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* * * * * Welcome to STN International * * * * *

| | | | |
|------|----|--------|--|
| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS | 2 | MAR 31 | IFICDB, IFIPAT, and IFIUIDB enhanced with new custom IPC display formats |
| NEWS | 3 | MAR 31 | CAS REGISTRY enhanced with additional experimental spectra |
| NEWS | 4 | MAR 31 | CA/CAPLUS and CASREACT patent number format for U.S. applications updated |
| NEWS | 5 | MAR 31 | LPCI now available as a replacement to LDPCI |
| NEWS | 6 | MAR 31 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |
| NEWS | 7 | APR 04 | STN AnaVist, Version 1, to be discontinued |
| NEWS | 8 | APR 15 | WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats |
| NEWS | 9 | APR 28 | EMBASE Controlled Term thesaurus enhanced |
| NEWS | 10 | APR 28 | IMSRESEARCH reloaded with enhancements |
| NEWS | 11 | MAY 30 | INPAFAMDB now available on STN for patent family searching |
| NEWS | 12 | MAY 30 | DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option |
| NEWS | 13 | JUN 06 | EPFULL enhanced with 260,000 English abstracts |
| NEWS | 14 | JUN 06 | KOREAPAT updated with 41,000 documents |
| NEWS | 15 | JUN 13 | USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications |
| NEWS | 16 | JUN 19 | CAS REGISTRY includes selected substances from web-based collections |
| NEWS | 17 | JUN 25 | CA/CAPLUS and USPAT databases updated with IPC reclassification data |
| NEWS | 18 | JUN 30 | AEROSPACE enhanced with more than 1 million U.S. patent records |
| NEWS | 19 | JUN 30 | EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations |
| NEWS | 20 | JUN 30 | STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in |
| NEWS | 21 | JUN 30 | STN AnaVist enhanced with database content from EPFULL |
| NEWS | 22 | JUL 28 | CA/CAPLUS patent coverage enhanced |
| NEWS | 23 | JUL 28 | EPFULL enhanced with additional legal status information from the epline Register |
| NEWS | 24 | JUL 28 | IFICDB, IFIPAT, and IFIUIDB reloaded with enhancements |
| NEWS | 25 | JUL 28 | STN Viewer performance improved |
| NEWS | 26 | AUG 01 | INPADOCDB and INPAFAMDB coverage enhanced |

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 15:59:10 ON 02 AUG 2008

=>

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 15:59:21 ON 02 AUG 2008

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 JUL 2008 HIGHEST RN 1037599-78-2
DICTIONARY FILE UPDATES: 31 JUL 2008 HIGHEST RN 1037599-78-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

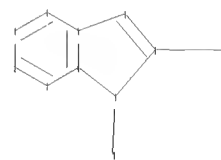
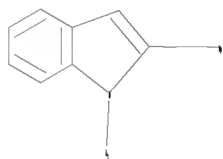
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

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```

chain nodes :
11 12
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
8-12 9-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
5-7 6-9 7-8 8-9 8-12 9-11
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
  
```

G1:H,CH3,OH

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:CLASS
12:Atom

L1 STRUCTURE UPLOADED

=> s 11

SAMPLE SEARCH INITIATED 15:59:36 FILE 'REGISTRY'

10/557537-Part I

SAMPLE SCREEN SEARCH COMPLETED - 183499 TO ITERATE

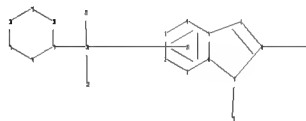
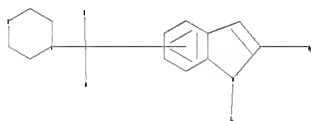
1.1% PROCESSED 2000 ITERATIONS 9 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **INCOMPLETE**
PROJECTED ITERATIONS: 3644767 TO 3695193
PROJECTED ANSWERS: 14790 TO 18238

L2 9 SEA SSS SAM L1

=>

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Documents\Stnexp\Queries\10557537-A.str



chain nodes :
11 12 20 21 22
ring nodes :
1 2 3 4 5 6 7 8 9 14 15 16 17 18 19
chain bonds :
8-12 9-11 19-20 20-21 20-22
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 14-15 14-19 15-16 16-17 17-18
18-19
exact/norm bonds :
5-7 6-9 7-8 8-9 8-12 9-11 14-15 14-19 15-16 16-17 17-18 18-19 19-20
exact bonds :
20-21 20-22
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:H,CH3,OH

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:CLASS
12:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS
22:CLASS 23:Atom

Generic attributes :

12:

Saturation : Unsaturated

Number of Carbon Atoms : 7 or more

Type of Ring System : Polycyclic

Element Count :

Node 12: Limited

N,N1

O,O0

S,S0

L3 STRUCTURE UPLOADED

=> s 13

SAMPLE SEARCH INITIATED 16:08:20 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 27924 TO ITERATE

7.2% PROCESSED 2000 ITERATIONS

0 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 548483 TO 568477

PROJECTED ANSWERS: 0 TO 0

L4 0 SEA SSS SAM L3

=> s 13 sss full

FULL SEARCH INITIATED 16:08:33 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 556853 TO ITERATE

100.0% PROCESSED 556853 ITERATIONS

177 ANSWERS

SEARCH TIME: 00.00.06

L5 177 SEA SSS FUL L3

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

185.26

185.47

FILE 'CAPLUS' ENTERED AT 16:08:47 ON 02 AUG 2008

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FILE COVERS 1907 - 2 Aug 2008 VOL 149 ISS 6
FILE LAST UPDATED: 2 Aug 2008 (20080802/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

=> s 15

L6 25 L5

=> d 16 1-25 bib abs hitstr

L6 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2008:771165 CAPLUS
DN 149:102715
TI Methods of treating cancer using IGF1r inhibitors
IN Wang, Yan; Zong, Chen; Seidel-Dugan, Cynthia; Wang, Yaolin; Yao, Siu-Long; Lu, Brian Der-Hua; Ladha, Mohamed H.
PA Schering Corporation, USA
SO PCT Int. Appl., 103pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| | ----- | ---- | ----- | ----- | ----- |
| PI | WO 2008076278 | A2 | 20080626 | WO 2007-US25398 | 20071211 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| PRAI | US 2006-874589P | P | 20061213 | | |
| | US 2006-870937P | P | 20061220 | | |

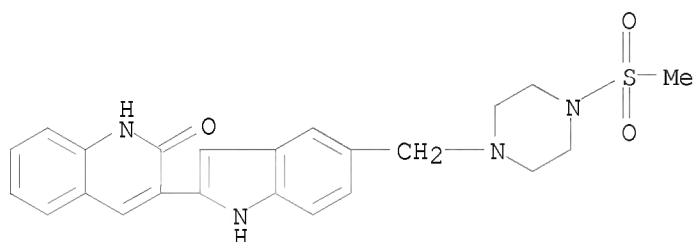
US 2007-946011P P 20070625
 US 2007-979274P P 20071011

AB The present invention provides IGF1R inhibitors and combinations thereof that are effective at treating or preventing cancer. More specifically the IGF1R inhibitors are pyrrolo[2,3-d]pyrimidine derivs. or antibodies. The IGF1R inhibitors can be used in combination with other anticancer therapies, antiemetic agents, antianemic agents, or antimucositis agents.

IT 335649-90-6
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (codrug; methods of treating cancer using IGF1R inhibitors)

RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



L6 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2008:502809 CAPLUS

DN 148:495784

TI Preparation of nitrogen-containing heterocycle compounds as JAK inhibitors

IN Amishiro, Nobuyoshi; Atsumi, Toshiyuki; Nakazato, Tomoyuki; Umehara, Hiroshi; Fujihara, Hiroaki; Shinohara, Fumikazu; Funahashi, Jun; Yamamoto, Junichiro; Yagi, Kaori

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO PCT Int. Appl., 358pp.
 CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2008047831 | A1 | 20080424 | WO 2007-JP70245 | 20071017 |
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| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| PRAI JP 2006-282088 | A | 20061017 | | |

OS MARPAT 148:495784
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [W = nitrogen atom or -CH-; X = -CO- or -CHR4-; R4 = H, hydroxy, (un)substituted alkyl, etc.; R1 = Q, etc.; Q1 = nitrogen atom or -CR8-; R8 = H, halo, nitro, etc.; Q2 = oxygen, sulfur atom or -NR15-; R15 = H, (un)substituted alkyl, (un)substituted cycloalkyl, etc.; R5, R6 = H, halo, nitro, etc.; R2, R3 = H, halo, nitro, etc.] or their pharmacol. acceptable salts were prepared Thus, a multi-step synthesis of compound II·HCl, starting from 7-amino-4-bromoisindolinone, was given. In JAK2 (Janus kinase 2) inhibition assays, the exemplified compound II·HCl showed activity of ≥50% at 1 μmol/L. Compds. I are claimed useful for the treatment of myeloproliferative disorders, immune diseases, etc.

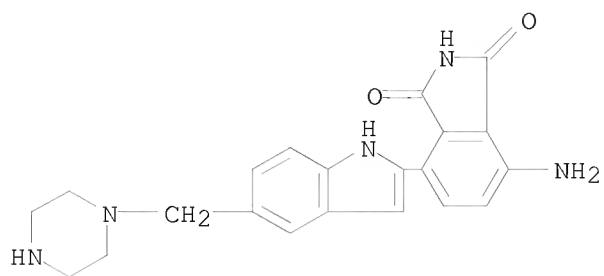
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1021342-23-3P 1021342-29-9P 1021342-31-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrogen-containing heterocycle compds. as JAK inhibitors)

RN 913383-62-7 CAPLUS

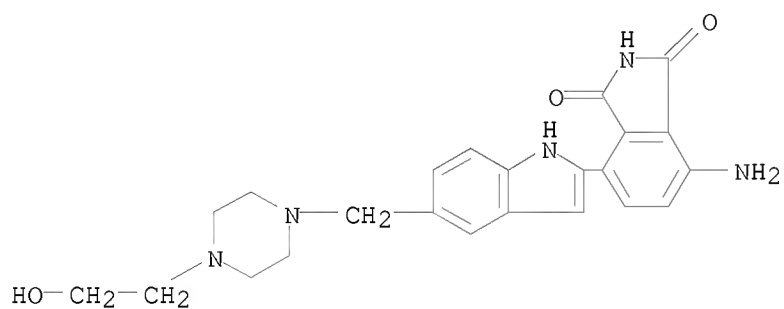
CN 1H-Isoindole-1,3(2H)-dione, 4-amino-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913383-63-8 CAPLUS

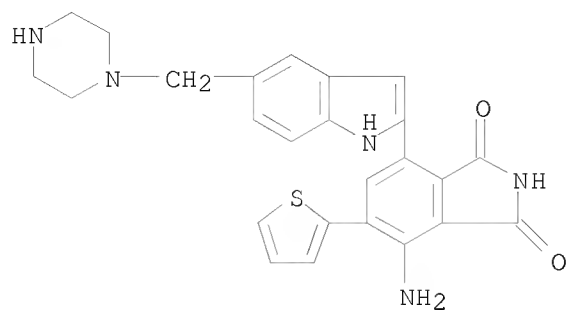
CN 1H-Isoindole-1,3(2H)-dione, 4-amino-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

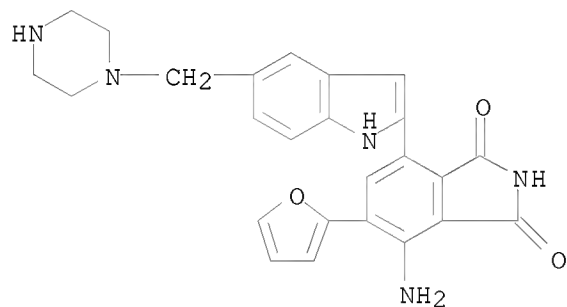
RN 913383-69-4 CAPLUS

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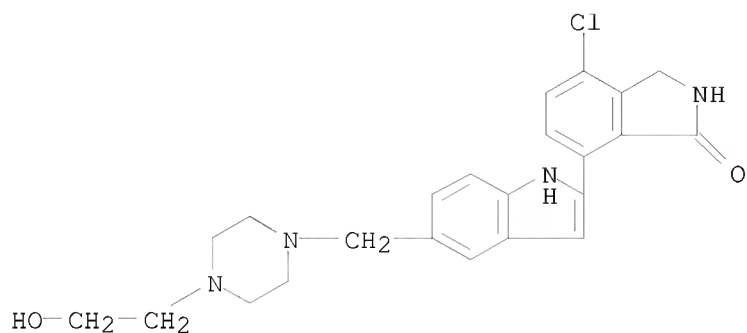
● 2 HCl

RN 913383-70-7 CAPLUS
 CN 1H-Isoindole-1,3(2H)-dione, 4-amino-5-(2-furanyl)-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



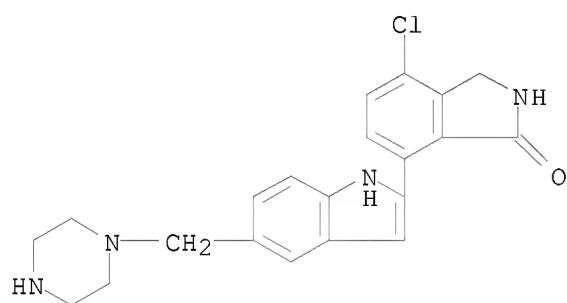
● 2 HCl

RN 913383-81-0 CAPLUS
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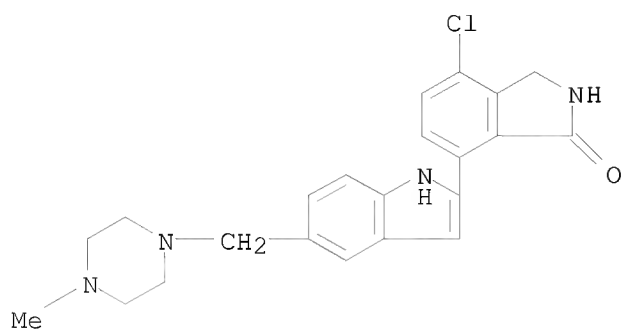
● 2 HCl

RN 913383-83-2 CAPLUS
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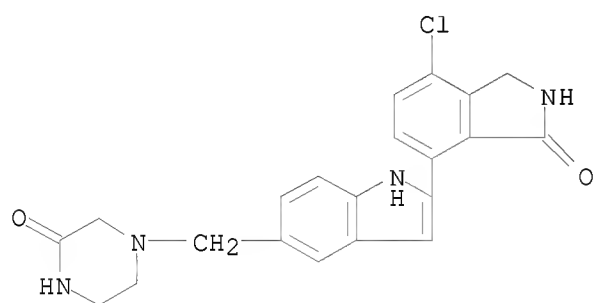
● 2 HCl

RN 913383-99-0 CAPLUS
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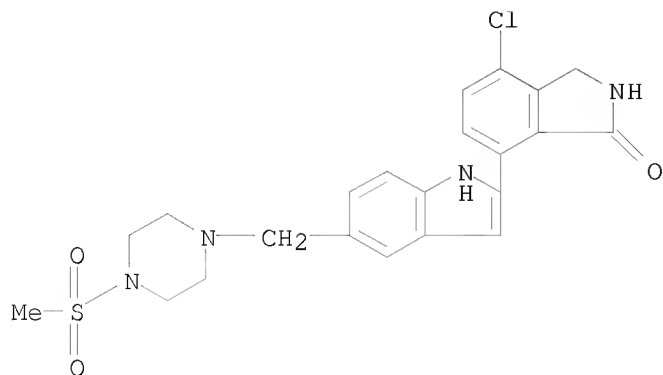
● 2 HCl

RN 913384-00-6 CAPLUS
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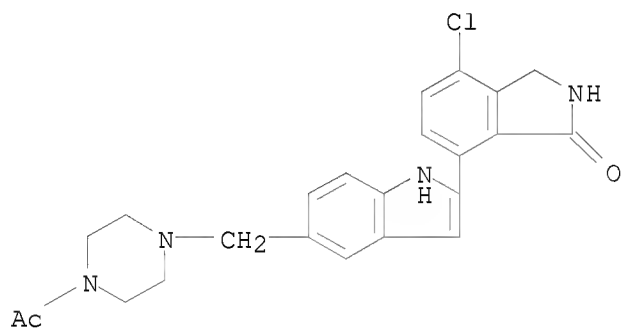
● HCl

RN 913384-11-9 CAPLUS
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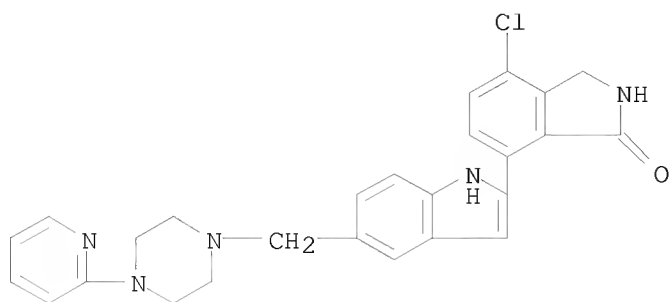
● HCl

RN 913384-12-0 CAPLUS
 CN 1H-Isoindol-1-one, 7-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-4-chloro-2,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)



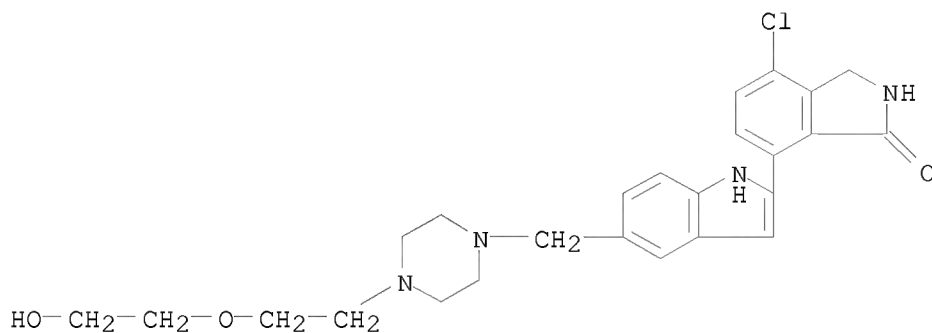
● HCl

RN 913384-47-1 CAPLUS
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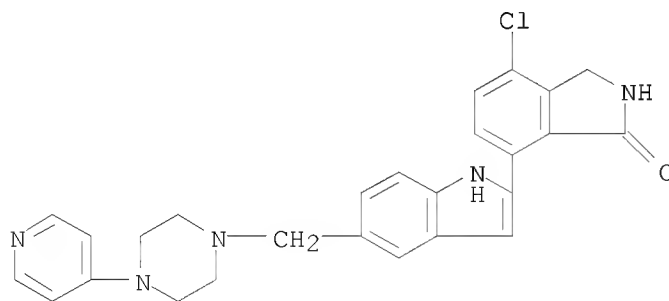
RN 913384-50-6 CAPLUS

CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-(2-hydroxyethoxy)ethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 913384-52-8 CAPLUS

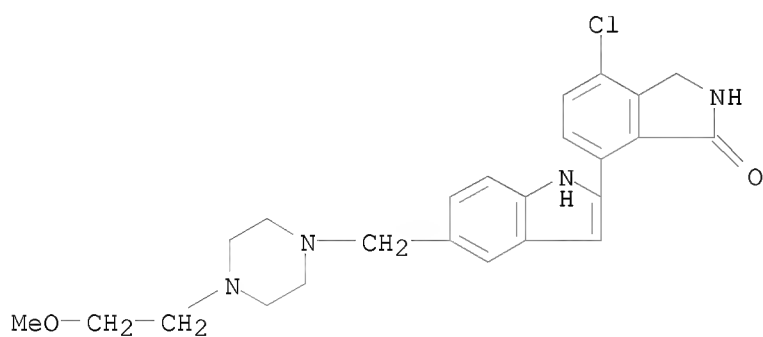
CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(4-pyridinyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



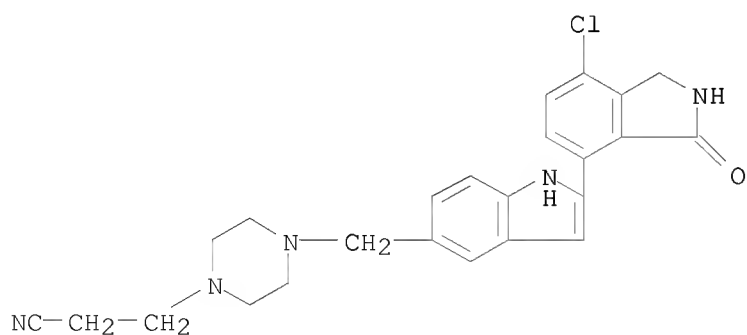
RN 913384-53-9 CAPLUS

CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-pyrimidinyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[4-(2-methoxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

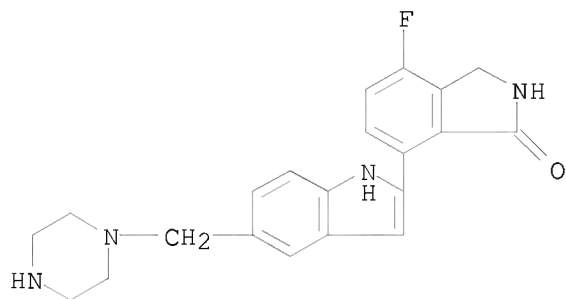


CN 1-Piperazinepropanenitrile, 4-[[2-(7-chloro-2,3-dihydro-3-oxo-1H-isoindol-4-yl)-1H-indol-5-yl]methyl]-, hydrochloride (1:2) (CA INDEX NAME)



CN 1H-Isoindol-1-one, 4-fluoro-2,3-dihydro-7-[5-(1-piperazinylmethyl)-1H-

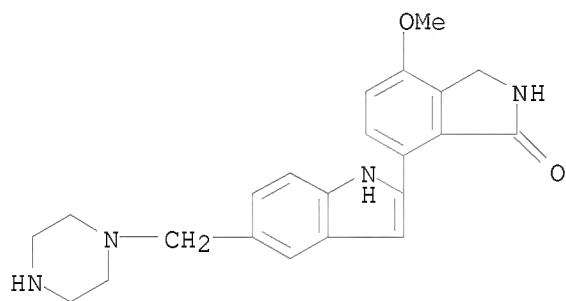
indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913384-92-6 CAPLUS

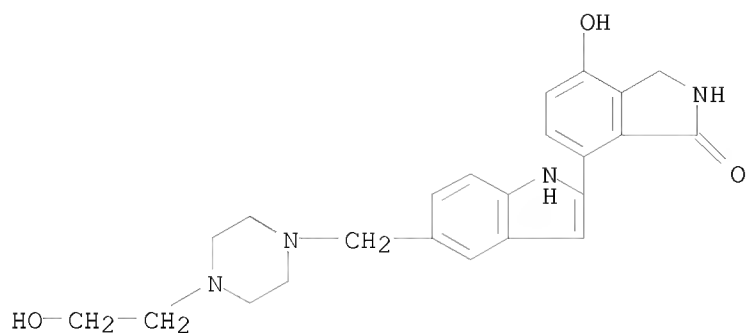
CN 1H-Isoindol-1-one, 2,3-dihydro-4-methoxy-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

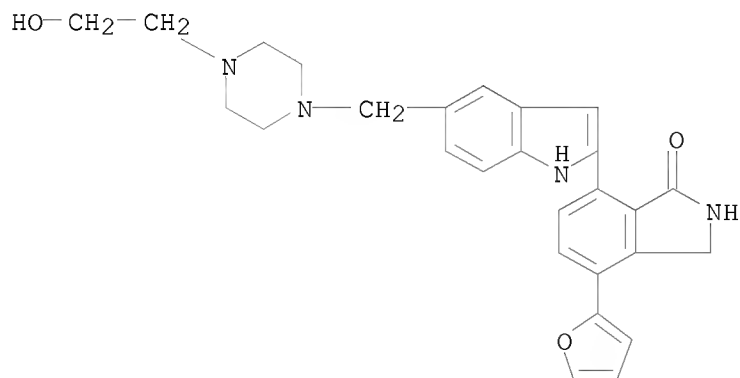
RN 913385-04-3 CAPLUS

CN 1H-Isoindol-1-one, 2,3-dihydro-4-hydroxy-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



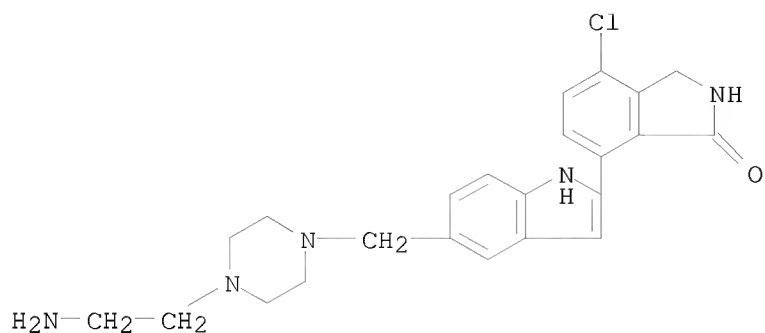
● 2 HCl

RN 913385-05-4 CAPLUS
 CN 1H-Isoindol-1-one, 4-(2-furanyl)-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



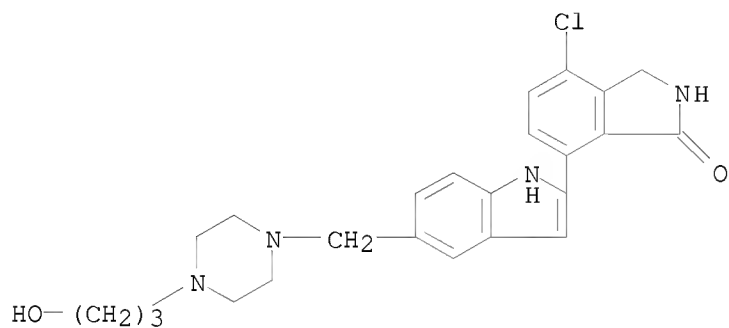
● 2 HCl

RN 913385-45-2 CAPLUS
 CN 1H-Isoindol-1-one, 7-[5-[[4-(2-aminoethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-4-chloro-2,3-dihydro-, hydrochloride (1:3) (CA INDEX NAME)



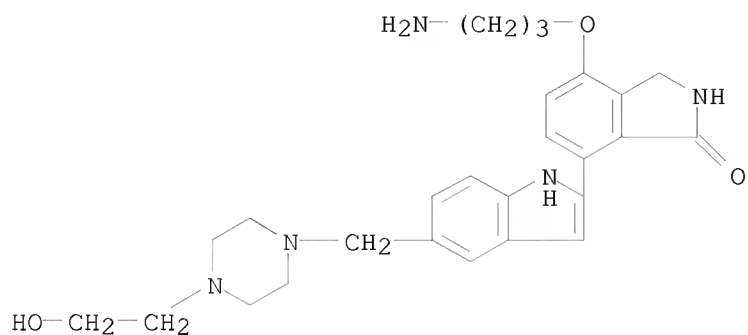
● 3 HCl

RN 913385-46-3 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(3-hydroxypropyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



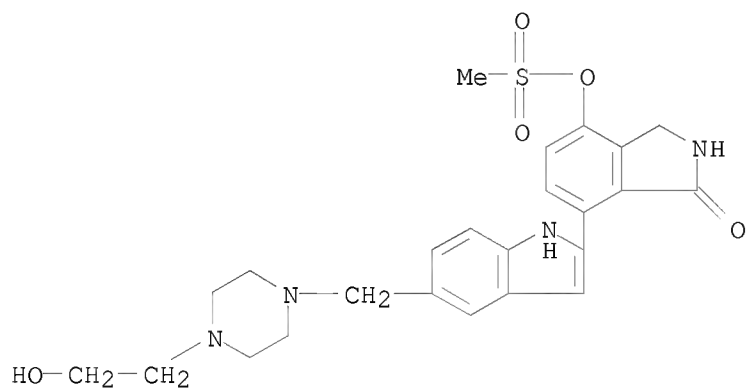
● 2 HCl

RN 913385-77-0 CAPLUS
 CN 1H-Isoindol-1-one, 4-(3-aminopropoxy)-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:3) (CA INDEX NAME)



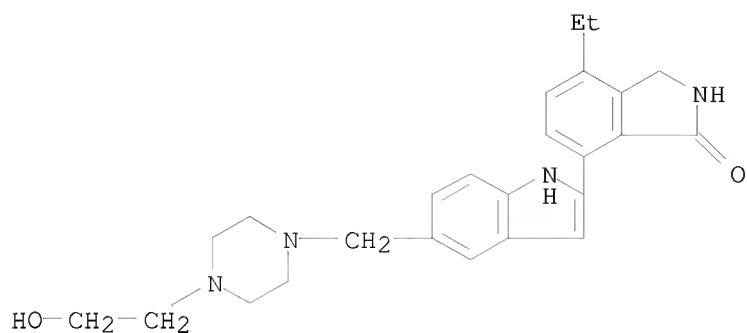
●3 HCl

RN 913386-46-6 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-4-[(methylsulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



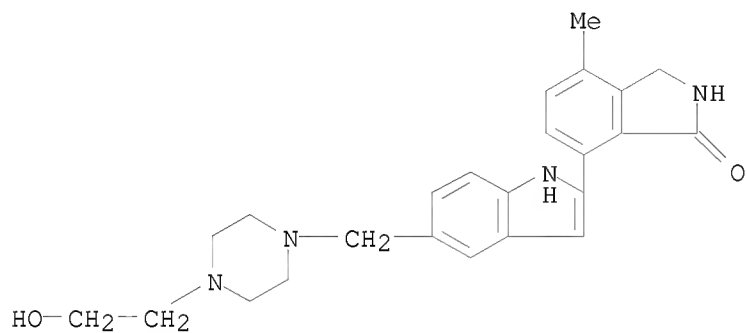
●2 HCl

RN 913386-59-1 CAPLUS
 CN 1H-Isoindol-1-one, 4-ethyl-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



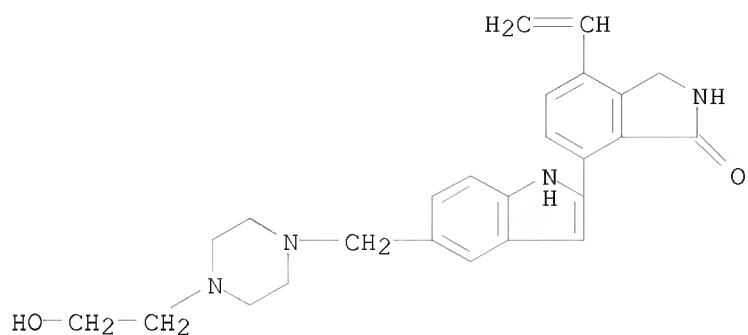
● 2 HCl

RN 913386-60-4 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-4-methyl-, hydrochloride (1:2) (CA INDEX NAME)



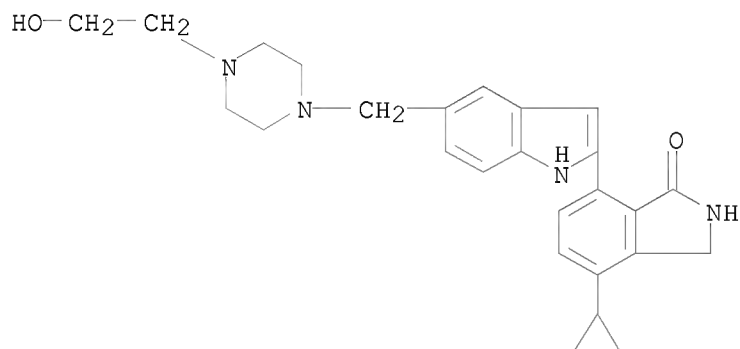
● 2 HCl

RN 913386-83-1 CAPLUS
 CN 1H-Isoindol-1-one, 4-ethenyl-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



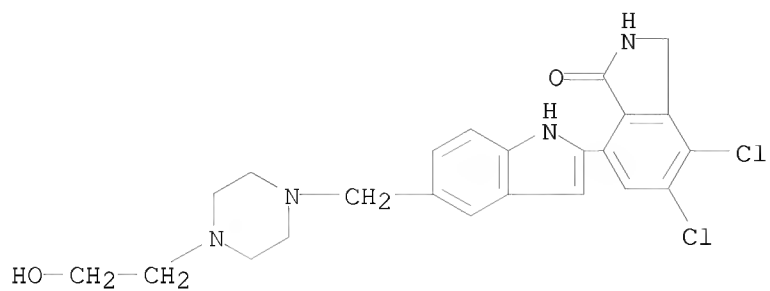
● 2 HCl

RN 913386-84-2 CAPLUS
 CN 1H-Isoindol-1-one, 4-cyclopropyl-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



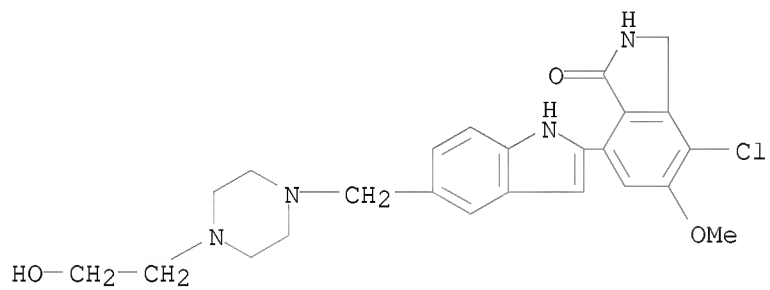
● 2 HCl

RN 913386-96-6 CAPLUS
 CN 1H-Isoindol-1-one, 4,5-dichloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



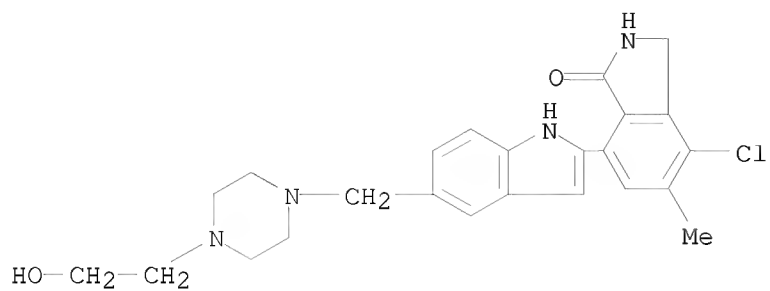
● 2 HCl

RN 913387-00-5 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methoxy-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

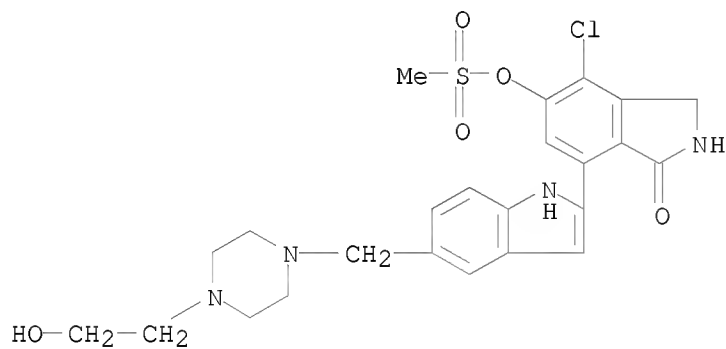
RN 913387-02-7 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methyl-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913387-07-2 CAPLUS

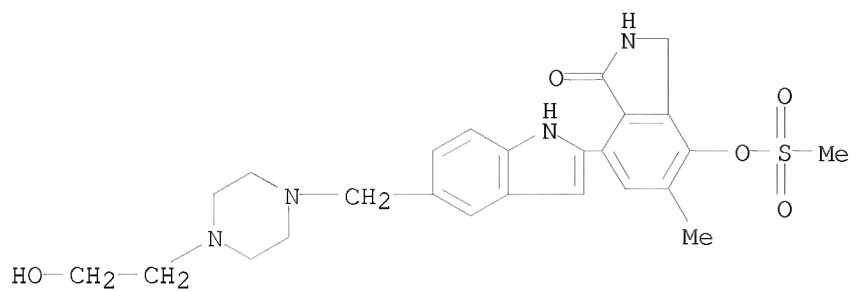
CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-[(methylsulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913387-13-0 CAPLUS

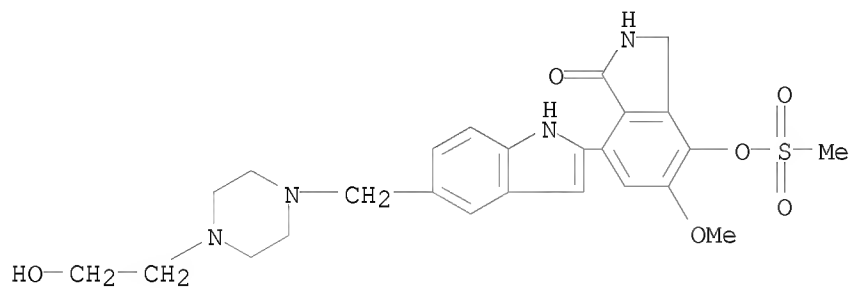
CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methyl-4-[(methylsulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913387-18-5 CAPLUS

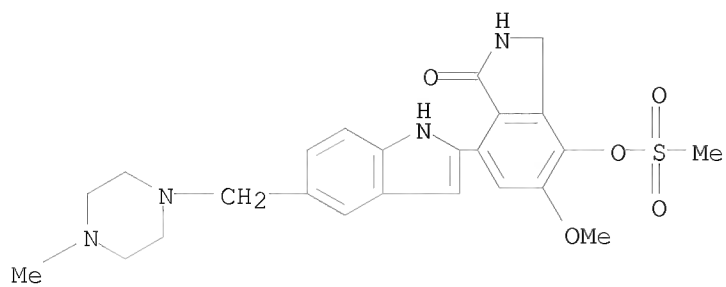
CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methoxy-4-[(methylsulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913387-25-4 CAPLUS

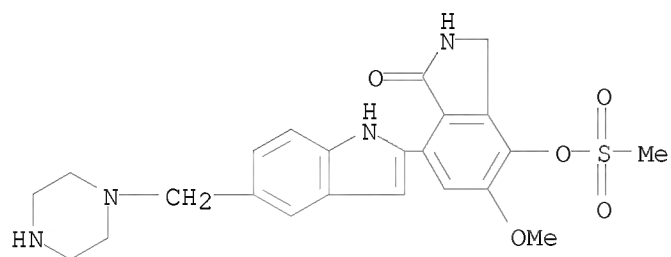
CN 1H-Isoindol-1-one, 2,3-dihydro-5-methoxy-7-[5-[[4-methyl-1-piperazinyl]methyl]-1H-indol-2-yl]-4-[(methylsulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913388-09-7 CAPLUS

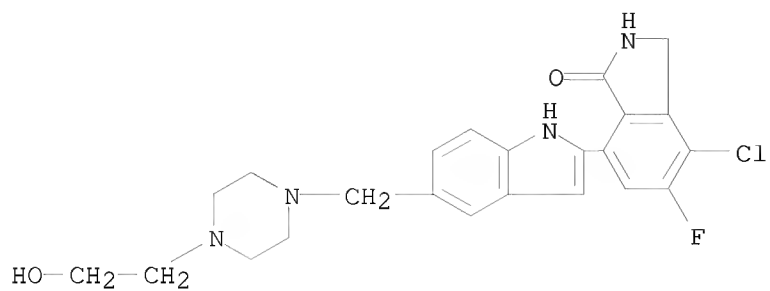
CN 1H-Isoindol-1-one, 2,3-dihydro-5-methoxy-4-[(methylsulfonyl)oxy]-7-[5-(1-methylpiperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

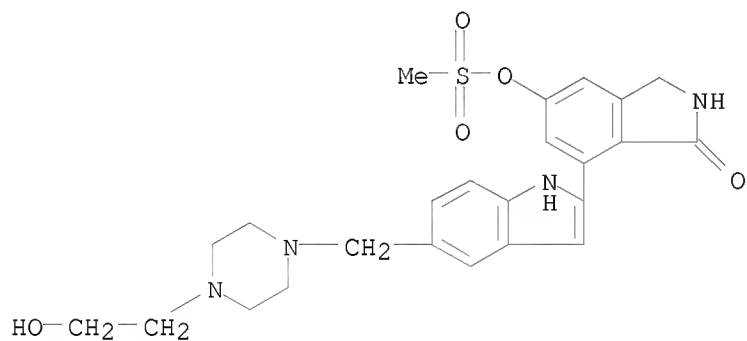
RN 913388-14-4 CAPLUS

CN 1H-Isoindol-1-one, 4-chloro-5-fluoro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



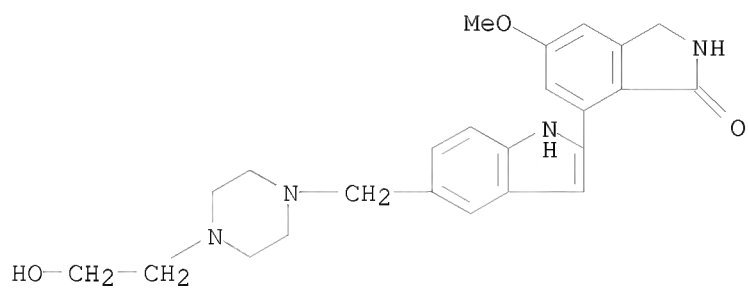
● 2 HCl

RN 1021340-74-8 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-[(methoxysulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



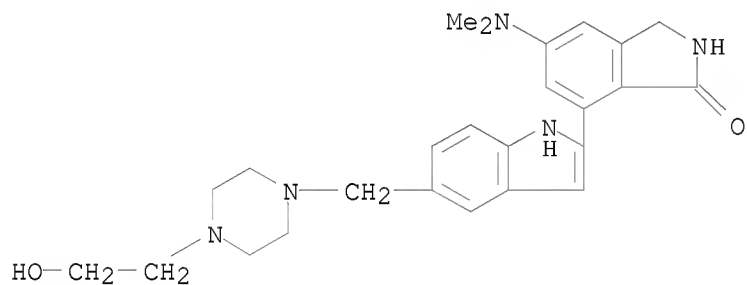
● 2 HCl

RN 1021340-75-9 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methoxy-, hydrochloride (1:2) (CA INDEX NAME)



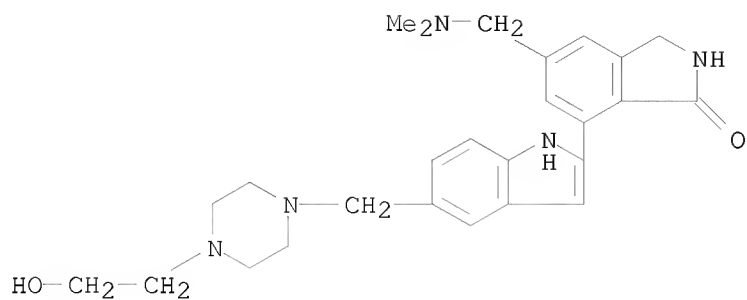
●2 HCl

RN 1021340-77-1 CAPLUS
 CN 1H-Isoindol-1-one, 5-(dimethylamino)-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:3) (CA INDEX NAME)



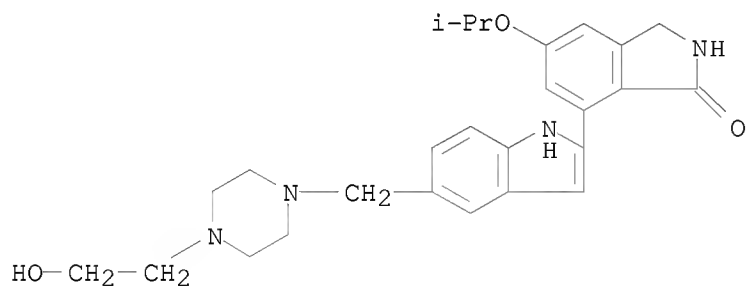
●3 HCl

RN 1021340-88-4 CAPLUS
 CN 1H-Isoindol-1-one, 5-[(dimethylamino)methyl]-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:3) (CA INDEX NAME)



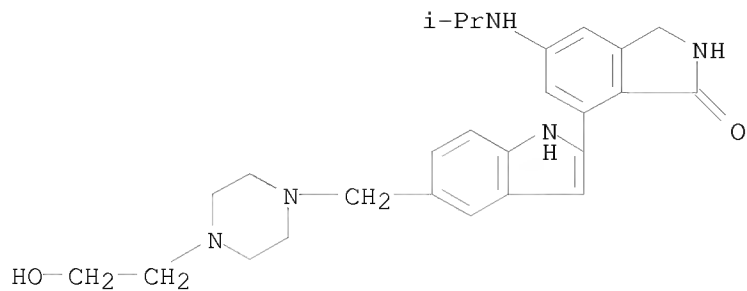
●3 HCl

RN 1021341-55-8 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-(1-methylethoxy)-, hydrochloride (1:2) (CA INDEX NAME)



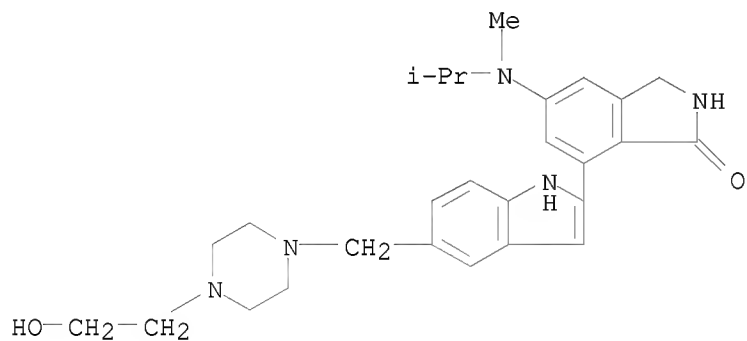
●2 HCl

RN 1021341-84-3 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-[(1-methylethyl)amino]-, hydrochloride (1:3) (CA INDEX NAME)



●3 HCl

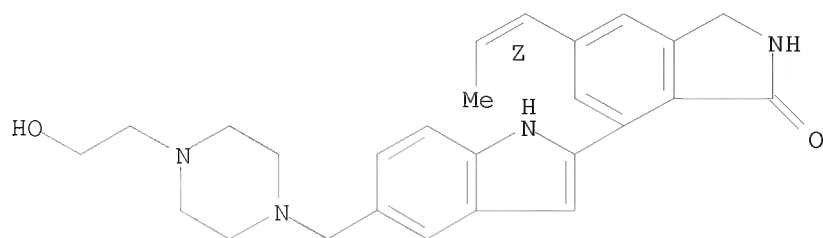
RN 1021341-85-4 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-[methyl(1-methylethyl)amino]-, hydrochloride (1:3) (CA INDEX NAME)



●3 HCl

RN 1021341-87-6 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-(1Z)-1-propen-1-yl-, hydrochloride (1:2) (CA INDEX NAME)

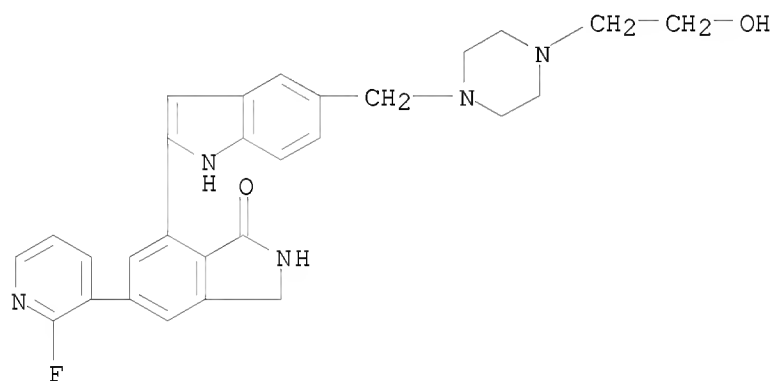
Double bond geometry as shown.



● 2 HCl

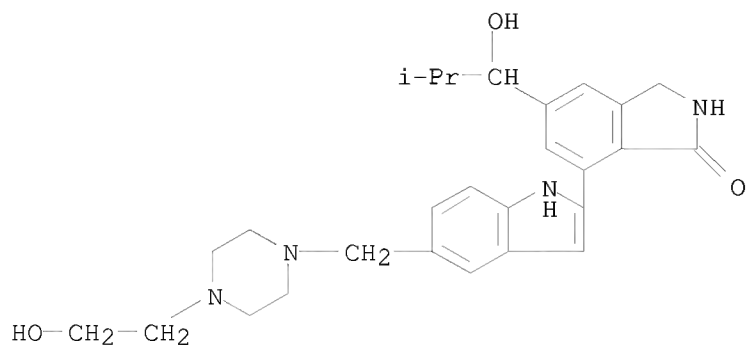
RN 1021342-02-8 CAPLUS

CN 1H-Isoindol-1-one, 5-(2-fluoro-3-pyridinyl)-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



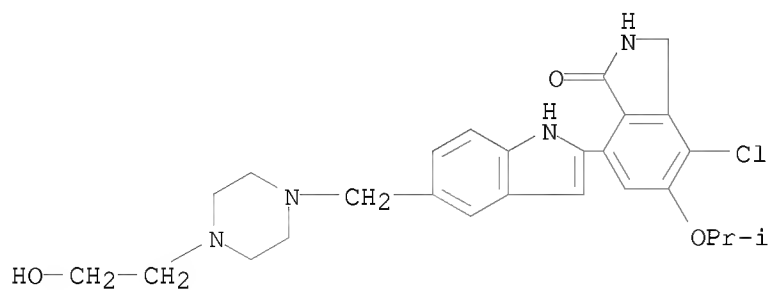
RN 1021342-08-4 CAPLUS

CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-(1-hydroxy-2-methylpropyl)-, hydrochloride (1:2) (CA INDEX NAME)



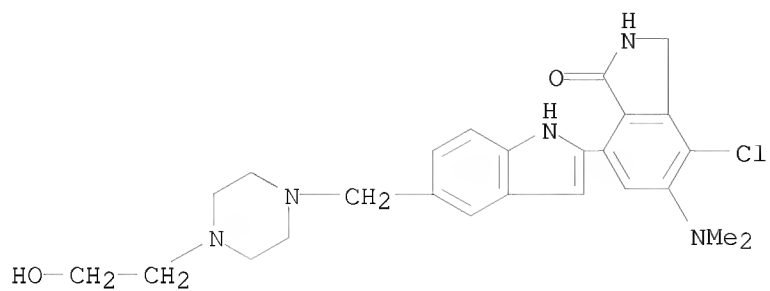
● 2 HCl

RN 1021342-11-9 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-(1-methylethoxy)-, hydrochloride (1:2) (CA INDEX NAME)



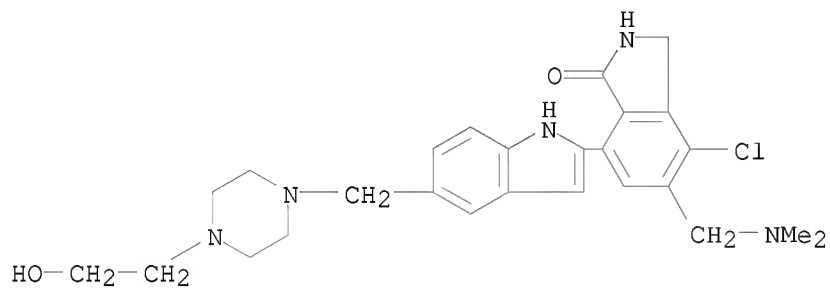
● 2 HCl

RN 1021342-17-5 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-5-(dimethylamino)-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



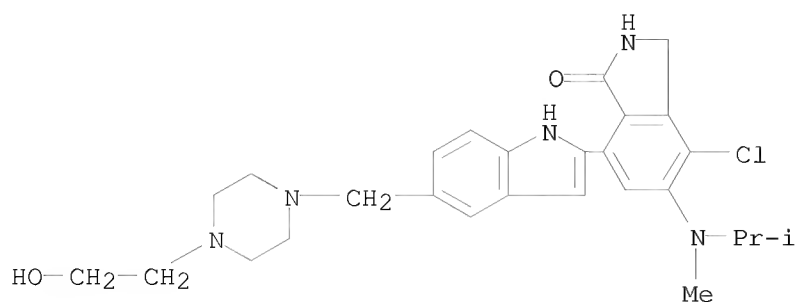
● 2 HCl

RN 1021342-19-7 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-5-[(dimethylamino)methyl]-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:3) (CA INDEX NAME)



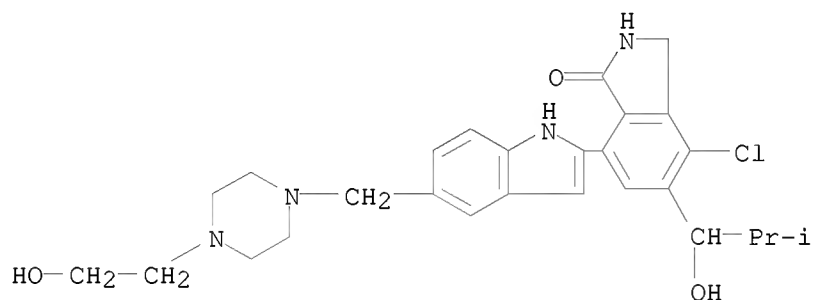
● 3 HCl

RN 1021342-20-0 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-[methyl(1-methylethyl)amino]-, hydrochloride (1:2) (CA INDEX NAME)



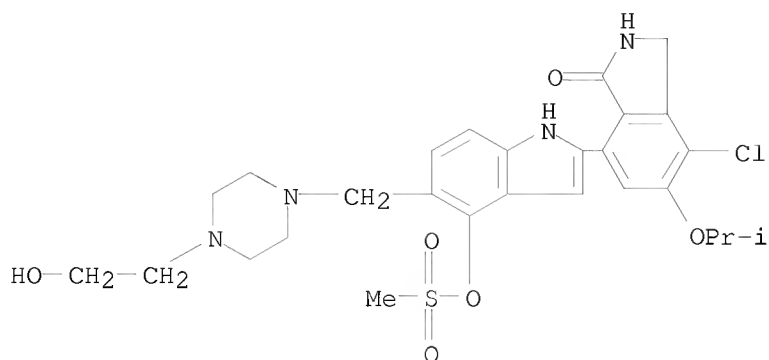
● 2 HCl

RN 1021342-23-3 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-(1-hydroxy-2-methylpropyl)-, hydrochloride (1:2) (CA INDEX NAME)



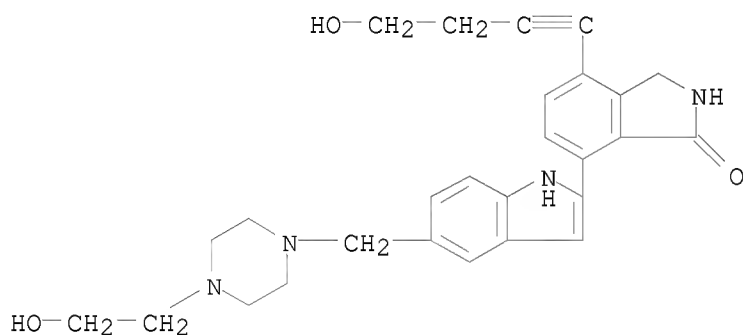
● 2 HCl

RN 1021342-29-9 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-(1-methylethoxy)-, hydrochloride (1:2) (CA INDEX NAME)



RN 1021342-31-3 CAPLUS

CN 1H-Isoindol-1-one, 2,3-dihydro-4-(4-hydroxy-1-butyn-1-yl)-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2008:43490 CAPLUS

DN 148:135980

TI Blood levels of insulin-like growth factor-binding protein 2 as a marker
for monitoring the effectiveness of inhibitors of insulin-like growth
factor I receptors in cancer therapy

IN Wang, Yan

PA Schering Corporation, USA

SO PCT Int. Appl., 133pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|---|----------|-----------------|----------|
| PI | WO 2008005469 | A2 | 20080110 | WO 2007-US15423 | 20070629 |
| | WO 2008005469 | A3 | 20080228 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, | | | |

GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
 KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
 MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
 PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
 GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20080112888 A1 20080515 US 2007-771454 20070629

PRAI US 2006-818004P P 20060630

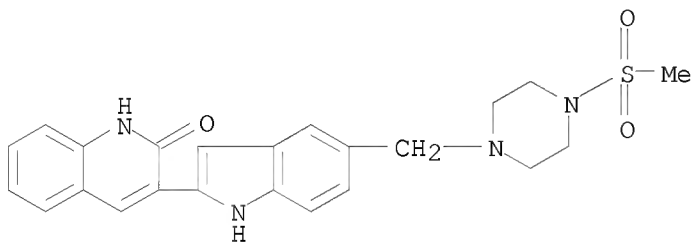
AB The present invention provides method for quickly and conveniently determining if a given treatment regimen of insulin-like growth factor I receptor (IGF1R) inhibitor is sufficient, e.g., to saturate IGF1 R receptors in the body of a subject. Blood levels of insulin-like growth factor-binding protein 2 (IGFBP2) are shown to be strongly correlated with the effectiveness of IGF1R receptor therapy. Several clin. relevant detns. may be made based on this point, including, for example, whether the dosage of the regimen is sufficient or should be increased. The relationship is demonstrated using animal xenograft models of neuroblastoma. Treatment with monoclonal antibodies to IGFR1 lowered the blood levels of IGFBP2. The level of IGFBP2 correlated with the tumor size.

IT 335649-90-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cancer therapy using; blood levels of IGBP2 as marker for monitoring effectiveness of inhibitors of IGF1 receptors in cancer therapy)

RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



L6 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2007:1310414 CAPLUS

DN 148:121566

TI Synthesis of an indole containing KDR kinase inhibitor by tandem Sonogashira coupling-5-endo-dig-cyclization as a key step

AU Palimkar, Sanjay S.; More, Vijaykumar S.; Kumar, P. Harish; Srinivasan, Kumar V.

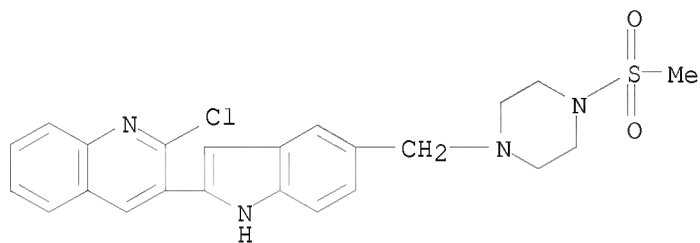
CS Division of Organic Chemistry, Technology, National Chemical Laboratory, Pune, Maharashtra, 411 008, India

SO Tetrahedron (2007), 63(51), 12786-12790

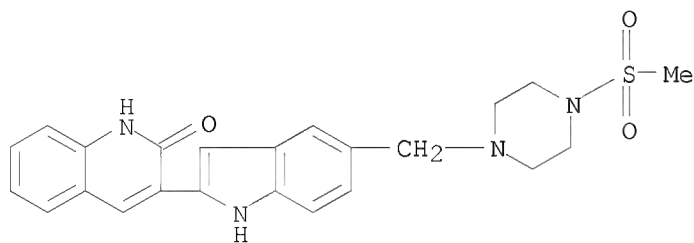
CODEN: TETRAB; ISSN: 0040-4020

PB Elsevier Ltd.

DT Journal
 LA English
 OS CASREACT 148:121566
 AB An efficient synthesis of the potent KDR kinase inhibitor 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]quinoline-2-(1H)-one using a Sonogashira coupling-5-endo-dig-cyclization strategy is described.
 IT 850171-34-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis of a potent KDR kinase inhibitor, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]quinoline-2-(1H)-one, by tandem Sonogashira coupling-5-endo-dig-cyclization)
 RN 850171-34-5 CAPLUS
 CN Quinoline, 2-chloro-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



IT 335649-90-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of a potent KDR kinase inhibitor, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]quinoline-2-(1H)-one, by tandem Sonogashira coupling-5-endo-dig-cyclization)
 RN 335649-90-6 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

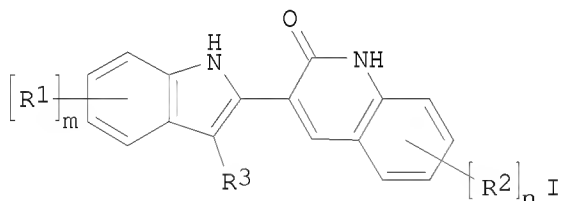
L6 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:816837 CAPLUS
 DN 147:400508
 TI Quinolinone inhibitors of checkpoint kinase CHK1 for treatment of cancer

IN Fraley, Mark E.; Garbaccio, Robert M.; Huang, Shaei Y.; Steen, Justin T.
 PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 80 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---------------------|--|----------|-----------------|----------|
| PI | WO 2007084135 | A2 | 20070726 | WO 2006-US2396 | 20060124 |
| | WO 2007084135 | A9 | 20071011 | | |
| | WO 2007084135 | A3 | 20080605 | | |
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| | RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | |
| | CA 2600914 | A1 | 20070726 | CA 2006-2600914 | 20060124 |
| | AU 2006324144 | A1 | 20070802 | AU 2006-324144 | 20060124 |
| | EP 1850847 | A2 | 20071107 | EP 2006-849351 | 20060124 |
| | R: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU | | | |
| | IN 2007DN05790 | A | 20070831 | IN 2007-DN5790 | 20070726 |
| PRAI | US 2005-647997P | P | 20050128 | | |
| | WO 2006-US2396 | W | 20060124 | | |
| OS | CASREACT 147:400508 | | | | |
| GI | | | | | |



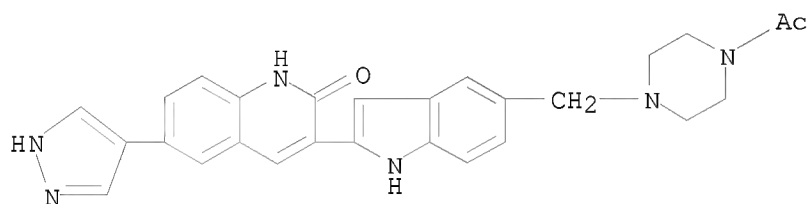
AB Substituted quinolinones I (R1,R2 = H, OH, CO2H, halo, alkyloxycarbonyl, alkenyloxycarbonyl, alkynyloxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, etc.; R3 = H, halo; m,n = 1-4), as well as pharmaceutically acceptable salts and stereoisomers, which inhibit checkpoint kinase CHK1 activity are disclosed. I may be used in treatment of cancer. The syntheses of a large number of I are described. The cloning of the cDNA for a splice variant of human CHK1 and the use of this enzyme for assaying inhibitory activity of I was also presented.

IT 916429-49-7P 916429-50-0P 916429-51-1P
 925688-77-3P 950759-76-9P 950759-77-0P
 950759-91-8P 950760-04-0P 950760-06-2P
 950760-07-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (quinolinone inhibitors of checkpoint kinase CHK1 for treatment of cancer)

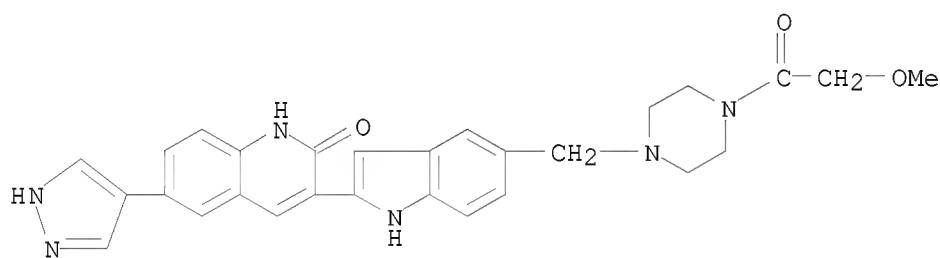
RN 916429-49-7 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(1H-pyrazol-4-yl)- (CA INDEX NAME)



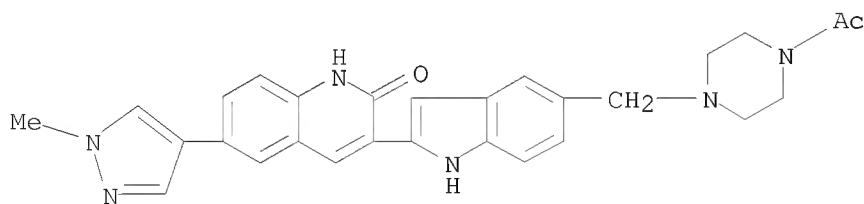
RN 916429-50-0 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(2-methoxyacetyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-6-(1H-pyrazol-4-yl)- (CA INDEX NAME)



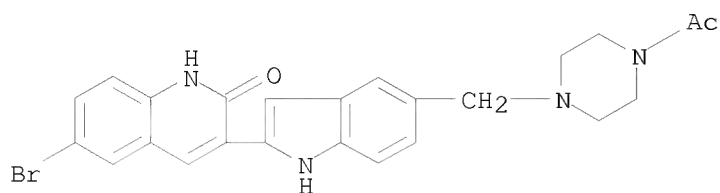
RN 916429-51-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(1-methyl-1H-pyrazol-4-yl)- (CA INDEX NAME)



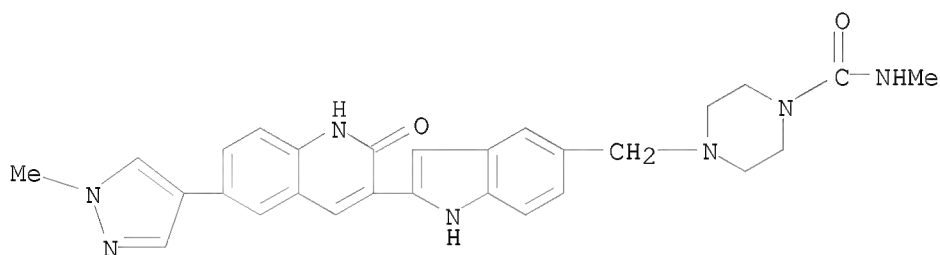
RN 925688-77-3 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-bromo- (CA INDEX NAME)



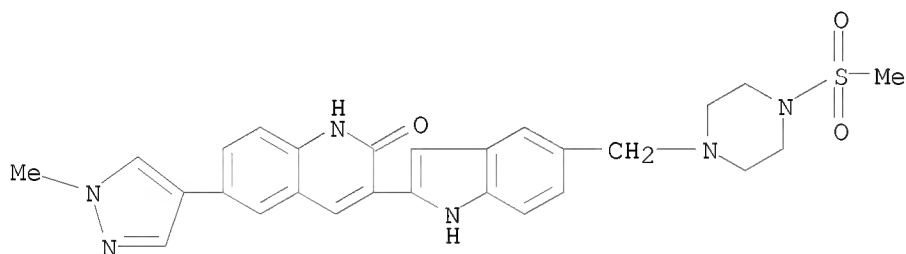
RN 950759-76-9 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[1,2-dihydro-6-(1-methyl-1H-pyrazol-4-yl)-2-oxo-3-quinolinyl]-1H-indol-5-yl]methyl]-N-methyl- (CA INDEX NAME)



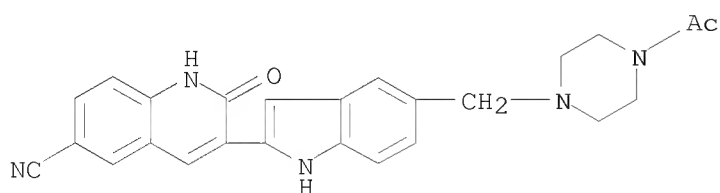
RN 950759-77-0 CAPLUS

CN 2(1H)-Quinolinone, 6-(1-methyl-1H-pyrazol-4-yl)-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 950759-91-8 CAPLUS

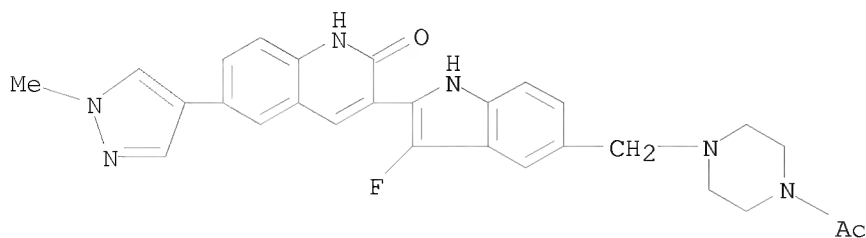
CN 6-Quinolinecarbonitrile, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-1,2-dihydro-2-oxo- (CA INDEX NAME)



RN 950760-04-0 CAPLUS

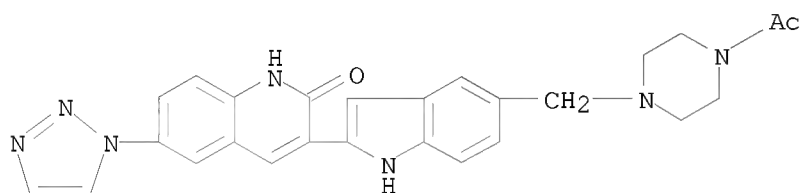
CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-3-fluoro-1H-indol-2-yl]- (CA INDEX NAME)

2-yl]-6-(1-methyl-1H-pyrazol-4-yl)- (CA INDEX NAME)



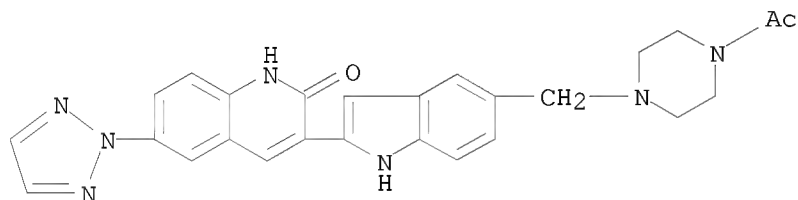
RN 950760-06-2 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(1H-1,2,3-triazol-1-yl)- (CA INDEX NAME)



RN 950760-07-3 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(2H-1,2,3-triazol-2-yl)- (CA INDEX NAME)



IT 950760-47-1 950760-48-2 950760-49-3

950760-51-7 950760-77-7 950760-82-4

950760-83-5

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinolinone inhibitors of checkpoint kinase CHK1 for treatment of cancer)

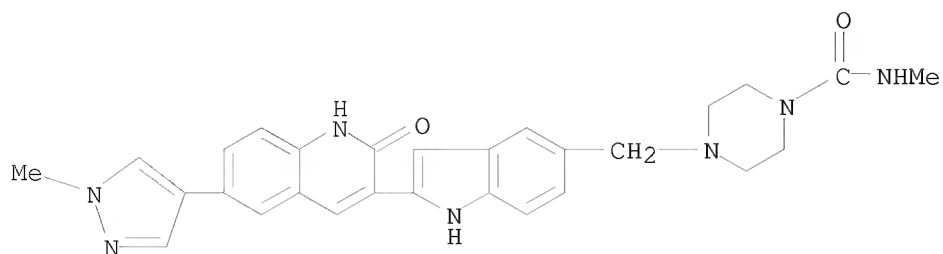
RN 950760-47-1 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[1,2-dihydro-6-(1-methyl-1H-pyrazol-4-yl)-2-oxo-3-quinolinyl]-1H-indol-5-yl]methyl]-N-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 950759-76-9

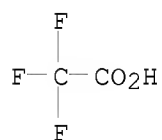
CMF C28 H29 N7 O2



CM 2

CRN 76-05-1

CMF C2 H F3 O2



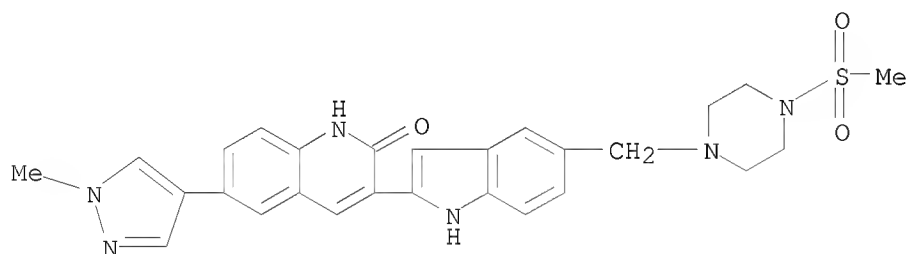
RN 950760-48-2 CAPLUS

CN 2(1H)-Quinolinone, 6-(1-methyl-1H-pyrazol-4-yl)-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 950759-77-0

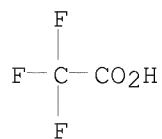
CMF C27 H28 N6 O3 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



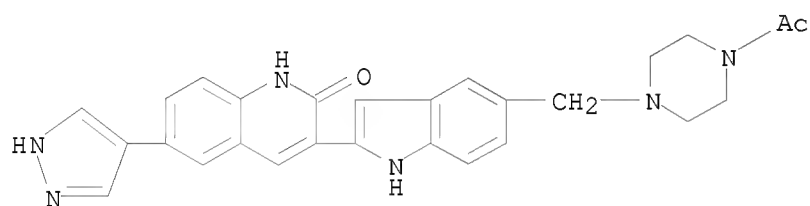
RN 950760-49-3 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(1H-pyrazol-4-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

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CRN 916429-49-7

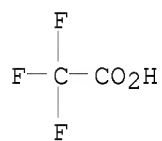
CMF C27 H26 N6 O2



CM 2

CRN 76-05-1

CMF C2 H F3 O2



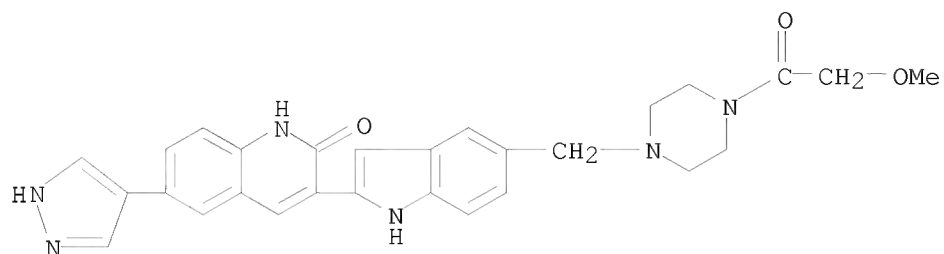
RN 950760-51-7 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(2-methoxyacetyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-6-(1H-pyrazol-4-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 916429-50-0

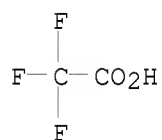
CMF C28 H28 N6 O3



CM 2

CRN 76-05-1

CMF C2 H F3 O2



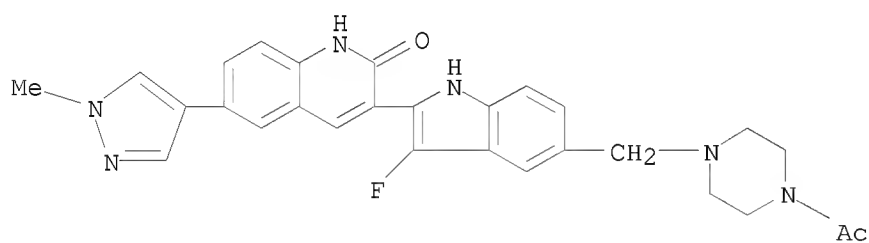
RN 950760-77-7 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-3-fluoro-1H-indol-2-yl]-6-(1-methyl-1H-pyrazol-4-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 950760-04-0

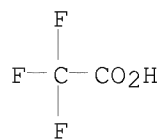
CMF C28 H27 F N6 O2



CM 2

CRN 76-05-1

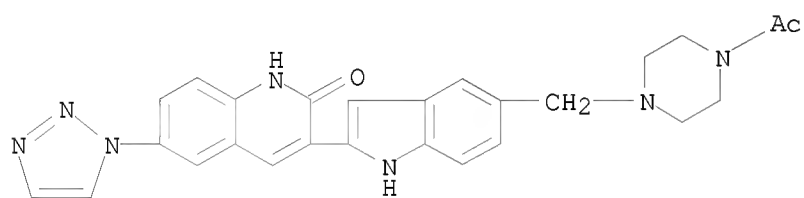
CMF C2 H F3 O2



RN 950760-82-4 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(1H-1,2,3-triazol-1-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

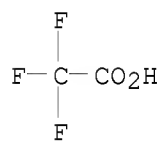
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CRN 950760-06-2
 CMF C26 H25 N7 O2



CM 2

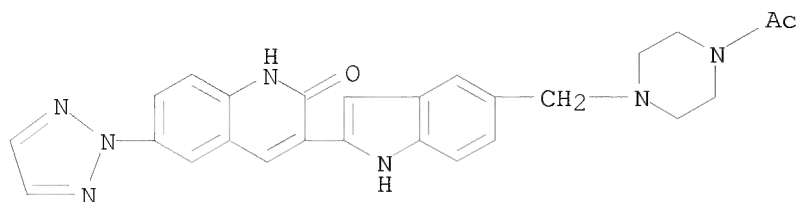
CRN 76-05-1
 CMF C2 H F3 O2



RN 950760-83-5 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(2H-1,2,3-triazol-2-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

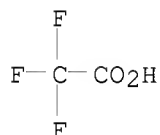
CRN 950760-07-3
 CMF C26 H25 N7 O2



CM 2

CRN 76-05-1

CMF C2 H F3 O2

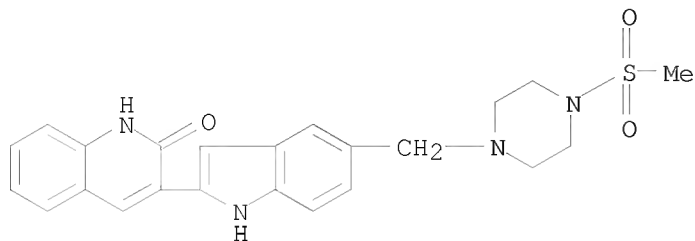


L6 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2007:82250 CAPLUS
 DN 146:337707
 TI Efficient Syntheses of KDR Kinase Inhibitors Using a Pd-Catalyzed Tandem C-N/Suzuki Coupling as the Key Step
 AU Fang, Yuan-Qing; Karisch, Robert; Lautens, Mark
 CS Davenport Chemistry Laboratories, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, Can.
 SO Journal of Organic Chemistry (2007), 72(4), 1341-1346
 CODEN: JOCEAH; ISSN: 0022-3263
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 146:337707
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

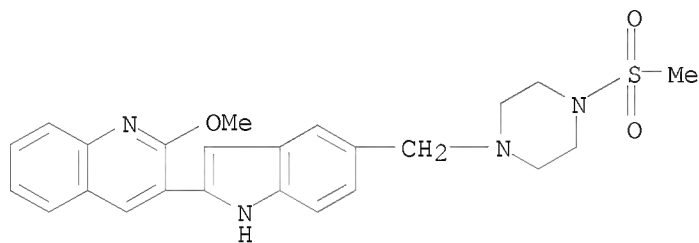
AB A family of four potent KDR kinase inhibitors containing an indol-2-yl quinolin-2-one structure, e.g. I, utilized a Pd-catalyzed tandem C-N and C-C coupling sequence. The key step in preparation of I involved the Pd(OAc)₂/(S)-Phos-catalyzed reaction of gem-dibromovinyl compound II with quinoline derivative III to give 86% indol-2-ylquinoline derivative IV.
 IT 415684-58-1P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of KDR kinase inhibitors using a Pd-catalyzed tandem C-N/Suzuki coupling as the key step)
 RN 415684-58-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

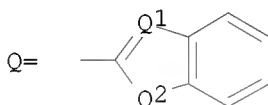
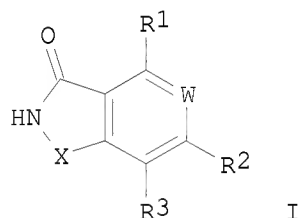
IT 796854-61-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of KDR kinase inhibitors using a Pd-catalyzed tandem C-N/Suzuki coupling as the key step)
 RN 796854-61-0 CAPLUS
 CN Quinoline, 2-methoxy-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:1123456 CAPLUS
 DN 145:454932
 TI Preparation of nitrogen-containing heterocyclic compounds as antitumor agents
 IN Murakata, Chikara; Amishiro, Nobuyoshi; Atsumi, Toshiyuki; Yamashita, Yoshinori; Takahashi, Takeshi; Nakai, Ryuichiro; Tagaya, Hisashi; Takahashi, Hiroko; Funahashi, Jun; Yamamoto, Junichiro; Fukuda, Yuichi
 PA Kyowa Hakko Kogyo Co., Ltd., Japan
 SO PCT Int. Appl., 531pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

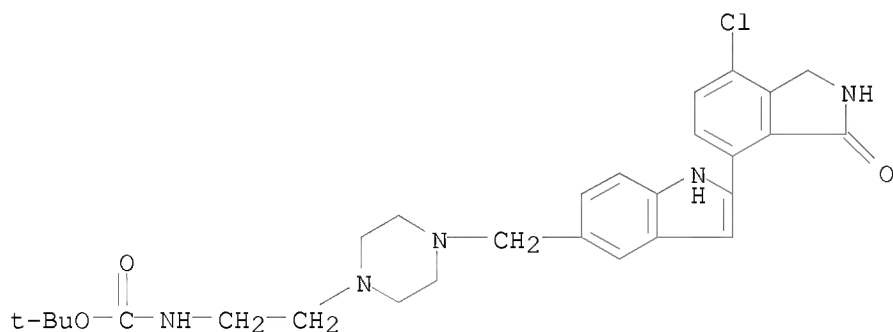
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|------------------|----------|
| PI | WO 2006112479 | A1 | 20061026 | WO 2006-JP308224 | 20060419 |
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| | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | AU 2006237920 | A1 | 20061026 | AU 2006-237920 | 20060419 |
| | CA 2610446 | A1 | 20061026 | CA 2006-2610446 | 20060419 |
| | EP 1880993 | A1 | 20080123 | EP 2006-745456 | 20060419 |
| | R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| | CN 101163675 | A | 20080416 | CN 2006-80013341 | 20071019 |
| | KR 2008011199 | A | 20080131 | KR 2007-726727 | 20071116 |
| PRAI | JP 2005-120953 | A | 20050419 | | |
| | WO 2006-JP308224 | W | 20060419 | | |
| OS | MARPAT 145:454932 | | | | |
| GI | | | | | |



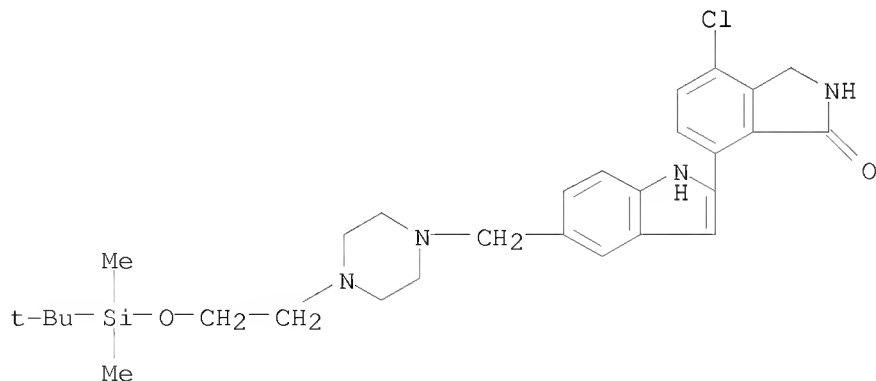
AB Nitrogen-containing heterocyclic compds. such as 7-(indol-2-yl)isoindolinone and 4-(indol-2-yl)-1,2-dihydro-1H-pyrrolo[3,4-c]pyridin-3-one derivs. [I; W = N, CH; X = CO, (un)substituted CH; R1 = Q; q1 = N, (un)substituted CH; Q2 = O, S, (un)substituted NH; R2, R3 R5, R6 = H, halo, NO2, HO, cyano, CO2H, each (un)substituted lower alkyl, cycloalkyl, aralkyl, lower alkenyl, lower alkynyl, aryl, heterocyclyl, lower alkanoyl, lower alkoxy carbonyl, aroyl, heteroaroyl, or HO, S(O)mR18; m = an integer of 0-2; R18 = H, HO, each (un)substituted lower alkoxy, lower alkyl, cycloalkyl, aralkyl, lower alkenyl, aryl, heterocyclyl, or NH2] or pharmacol. acceptable salts thereof are prepared These compds. are useful as protein kinase inhibitors, in particular fibroblast growth factor receptor (FGFR) inhibitors, Aurora kinase inhibitors, and FMS-like tyrosine kinase-3 (FLT-3) inhibitors, and thereby as antitumor agents for treatment of hematopoietic tumors, in particular leukemia, multiple myeloma, and lymphoma. Thus, reductive alkylation of 1-(2-hydroxyethyl)piperazine with 4-chloro-7-[1-(tert-butoxycarbonyl)-5-

formylindol-2-yl]isoindolinone using sodium triacetoxyborohydride in a mixture of AcOH and MeCN followed by treatment with HCl/EtOAc gave 4-chloro-7-(1H-5-[4-(2-hydroxyethyl)piperazin-1-ylmethyl]indol-2-yl)isoindolinone dihydrochloride (II). II at 10 μ M inhibited $\geq 50\%$ human FGFR3 expressed in insect cells, human multiple myeloma KMS-11 cells, and human stomach cancer cells KATO-III.

- IT 913390-38-2P, 4-Chloro-7-[5-[[4-[2-[(tert-butoxycarbonyl)amino]ethyl]piperazin-1-yl]methyl]indol-2-yl]isoindolinone
 913390-39-3P, 4-Chloro-7-[5-[[4-[2-[(tert-butyl)dimethylsilyl]oxy]ethyl]piperazin-1-yl]methyl]indol-2-yl]isoindolinone
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of nitrogen-containing heterocyclic compds. as protein kinase inhibitors and antitumor agents)
- RN 913390-38-2 CAPLUS
 CN Carbamic acid, [2-[4-[[2-(7-chloro-2,3-dihydro-3-oxo-1H-isoindol-4-yl)-1H-indol-5-yl]methyl]-1-piperazinyl]ethyl]-, 1,1-dimethylethyl ester (9CI)
 (CA INDEX NAME)



- RN 913390-39-3 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-7-[5-[[4-[2-[[1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-1-piperazinyl]methyl]-1H-indol-2-yl]-2,3-dihydro- (CA INDEX NAME)



- IT 913383-62-7P, 3-Amino-6-[1H-5-[(piperazin-1-yl)methyl]indol-2-

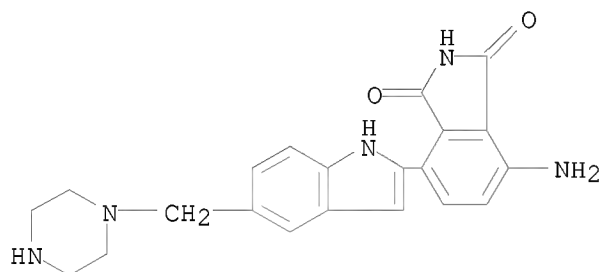
yl]phthalimide dihydrochloride 913383-63-8P,
3-Amino-6-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]phthalimide dihydrochloride 913383-69-4P,
3-Amino-4-(thiophen-2-yl)-6-[1H-5-[(piperazin-1-yl)methyl]indol-2-yl]phthalimide dihydrochloride 913383-70-7P,
3-Amino-4-(furan-2-yl)-6-[1H-5-[(piperazin-1-yl)methyl]indol-2-yl]phthalimide dihydrochloride 913383-81-0P,
4-Chloro-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913383-83-2P,
4-Chloro-7-[1H-5-[(piperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913383-99-0P, 4-Chloro-7-[1H-5-[[4-methylpiperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913384-00-6P, 4-Chloro-7-[1H-5-[(3-oxopiperazin-1-yl)methyl]indol-2-yl]isoindolinone monohydrochloride 913384-11-9P,
4-Chloro-7-[1H-5-[[4-(methanesulfonyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone monohydrochloride 913384-12-0P,
4-Chloro-7-[1H-5-[[4-(4-acetylpiperazin-1-yl)methyl]indol-2-yl]isoindolinone monohydrochloride 913384-47-1P, 4-Chloro-7-[1H-5-[[4-(pyridin-2-yl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone 913384-50-6P,
4-Chloro-7-[1H-5-[[4-[2-(2-hydroxyethoxy)ethyl]piperazin-1-yl]methyl]indol-2-yl]isoindolinone 913384-52-8P, 4-Chloro-7-[1H-5-[[4-(pyridin-4-yl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone 913384-53-9P,
4-Chloro-7-[1H-5-[[4-(pyrimidin-2-yl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone 913384-54-0P, 4-Chloro-7-[1H-5-[[4-(2-methoxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone 913384-87-9P, 4-Chloro-7-[1H-5-[[4-(2-cyanoethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913384-91-5P,
4-Fluoro-7-[1H-5-[(piperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913384-92-6P, 4-Methoxy-7-[1H-5-[(piperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913385-04-3P,
4-Hydroxy-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913385-05-4P,
4-(Furan-2-yl)-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913385-45-2P,
4-Chloro-7-[1H-5-[[4-(2-aminoethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone trihydrochloride 913385-46-3P,
4-Chloro-7-[1H-5-[[4-(3-hydroxypropyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913385-77-0P,
4-(3-Aminopropoxy)-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone trihydrochloride 913386-46-6P,
4-[(Methanesulfonyl)oxy]-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913386-59-1P,
4-Ethyl-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913386-60-4P,
4-Methyl-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913386-83-1P,
4-Vinyl-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913386-84-2P,
4-Cyclopropyl-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913386-96-6P,
4,5-Dichloro-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913387-00-5P,
4-Chloro-5-methoxy-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913387-02-7P,
4-Chloro-5-methyl-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl]methyl]indol-2-yl]isoindolinone dihydrochloride 913387-07-2P,
4-Chloro-5-[(methanesulfonyl)oxy]-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-

yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913387-13-0P,
 4-[(Methylsulfonyl)oxy]-5-methyl-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913387-18-5P,
 4-[(Methylsulfonyl)oxy]-5-methoxy-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913387-25-4P,
 4-[(Methylsulfonyl)oxy]-5-methoxy-7-[1H-5-[(4-methylpiperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913388-09-7P,
 4-[(Methylsulfonyl)oxy]-5-methoxy-7-[1H-5-[(piperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride 913388-14-4P,
 4-Chloro-5-fluoro-7-[1H-5-[[4-(2-hydroxyethyl)piperazin-1-yl)methyl]indol-2-yl]isoindolinone dihydrochloride
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrogen-containing heterocyclic compds. as protein kinase inhibitors and antitumor agents)

RN 913383-62-7 CAPLUS

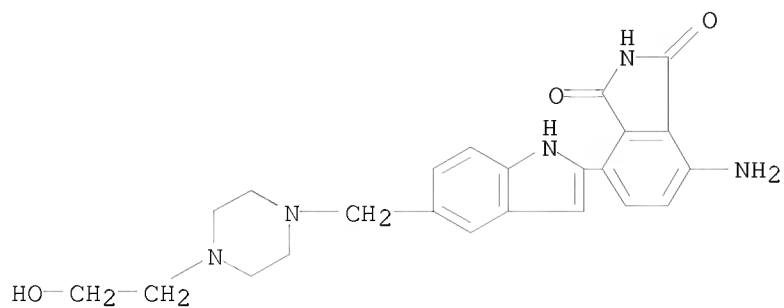
CN 1H-Isoindole-1,3(2H)-dione, 4-amino-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

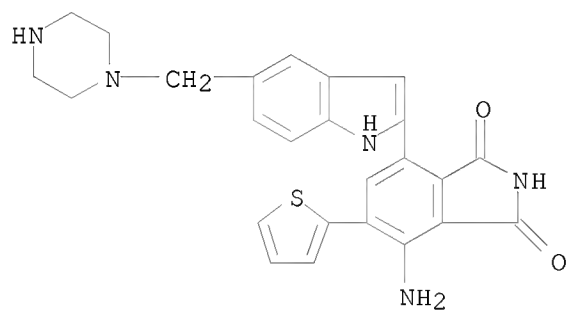
RN 913383-63-8 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 4-amino-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



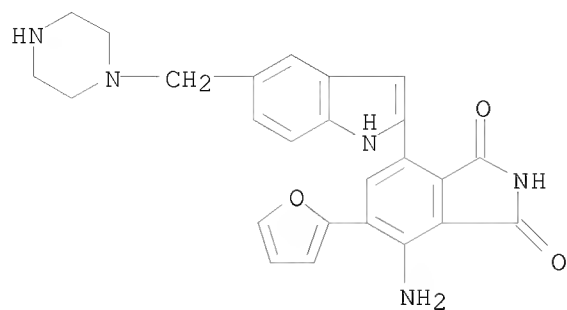
● 2 HCl

RN 913383-69-4 CAPLUS
 CN 1H-Isoindole-1,3(2H)-dione, 4-amino-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-5-(2-thienyl)-, hydrochloride (1:2) (CA INDEX NAME)



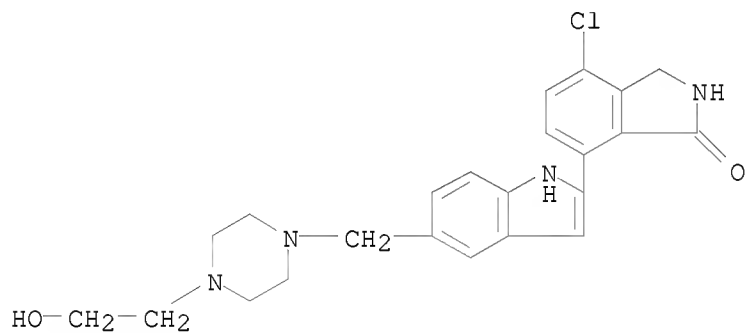
● 2 HCl

RN 913383-70-7 CAPLUS
 CN 1H-Isoindole-1,3(2H)-dione, 4-amino-5-(2-furanyl)-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



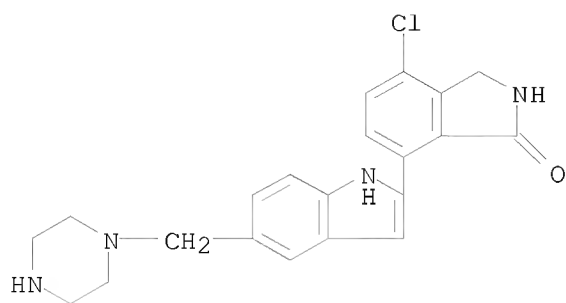
● 2 HCl

RN 913383-81-0 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



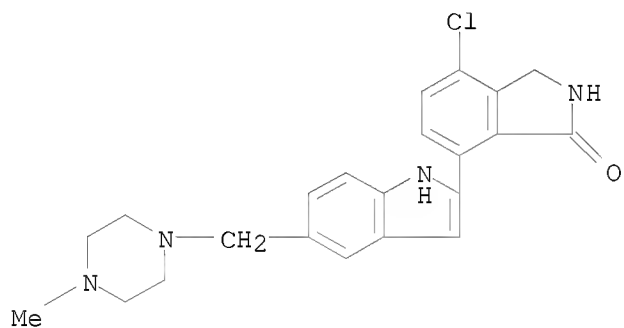
● 2 HCl

RN 913383-83-2 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



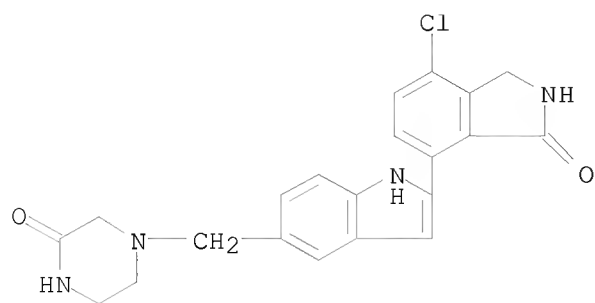
● 2 HCl

RN 913383-99-0 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[(4-methyl-1-piperazinyl)methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



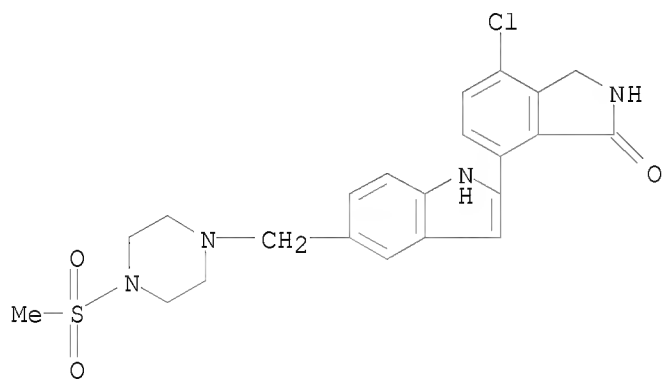
● 2 HCl

RN 913384-00-6 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[(3-oxo-1-piperazinyl)methyl]-1H-indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)



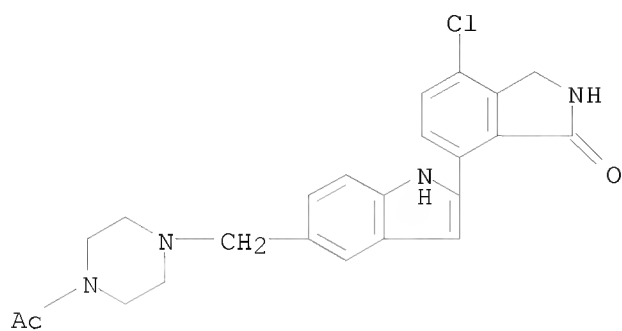
● HCl

RN 913384-11-9 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)



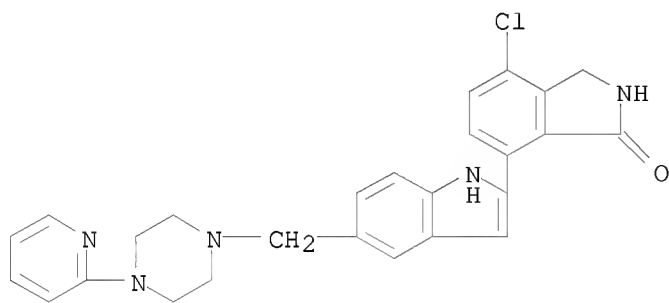
● HCl

RN 913384-12-0 CAPLUS
 CN 1H-Isoindol-1-one, 7-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-4-chloro-2,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)

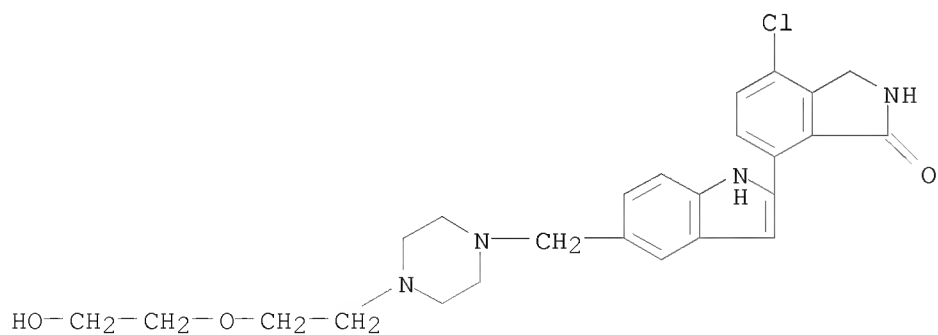


● HCl

RN 913384-47-1 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-pyridinyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



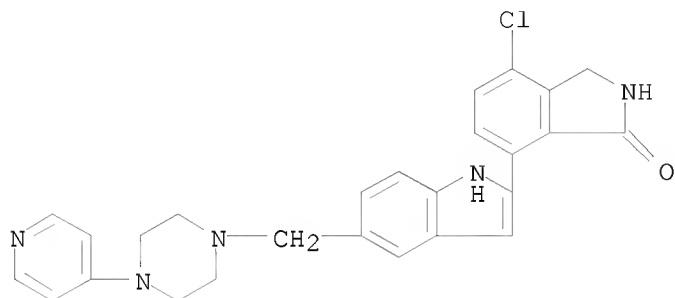
RN 913384-50-6 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



10/557537-Part I

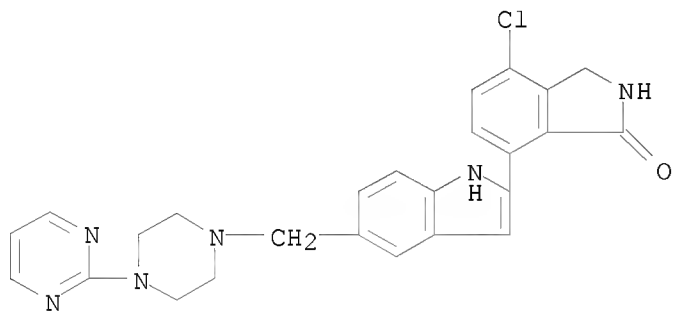
RN 913384-52-8 CAPLUS

CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(4-pyridinyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



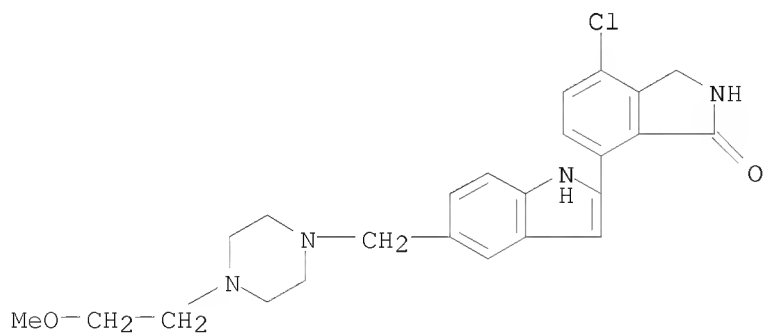
RN 913384-53-9 CAPLUS

CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-pyrimidinyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 913384-54-0 CAPLUS

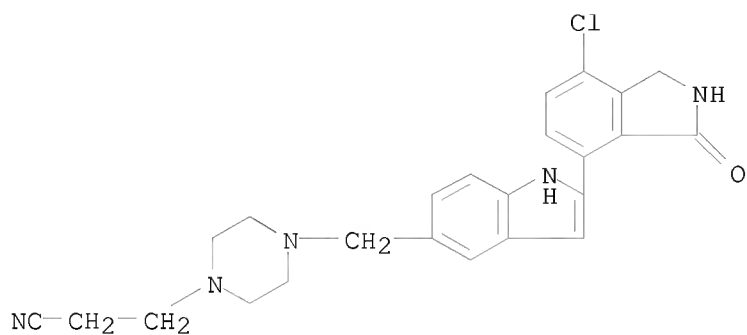
CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-methoxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 913384-87-9 CAPLUS

CN 1-Piperazinepropanenitrile, 4-[[2-(7-chloro-2,3-dihydro-3-oxo-1H-isoin-1-one

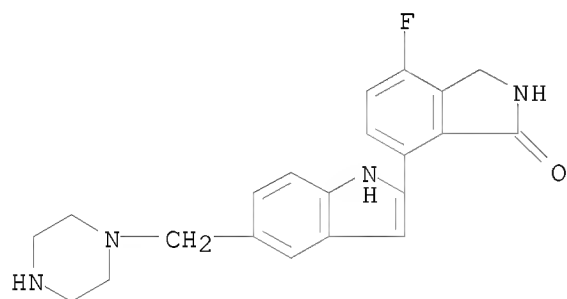
4-yl)-1H-indol-5-yl)methyl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913384-91-5 CAPLUS

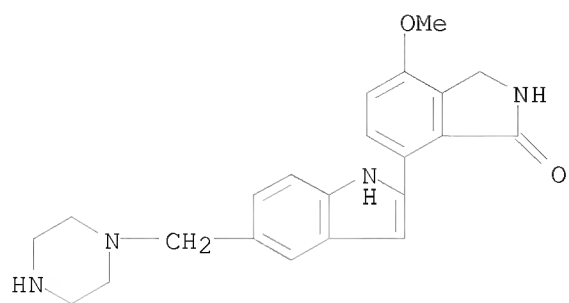
CN 1H-Isoindol-1-one, 4-fluoro-2,3-dihydro-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

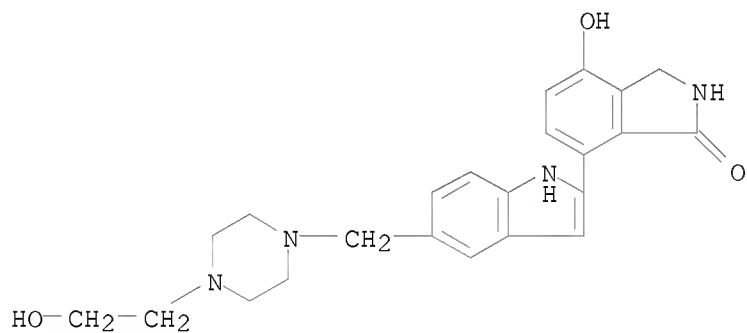
RN 913384-92-6 CAPLUS

CN 1H-Isoindol-1-one, 2,3-dihydro-4-methoxy-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



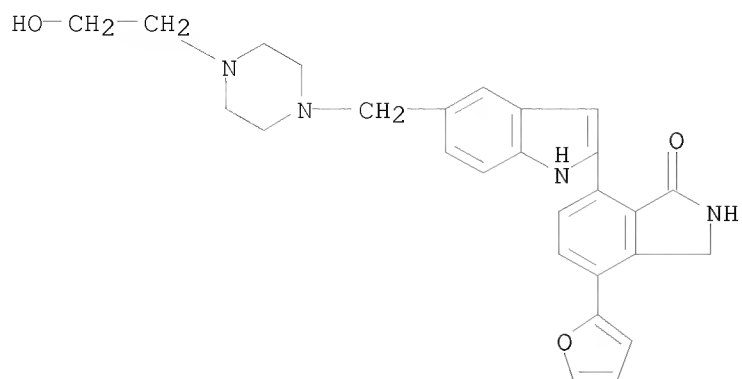
●2 HCl

RN 913385-04-3 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-4-hydroxy-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



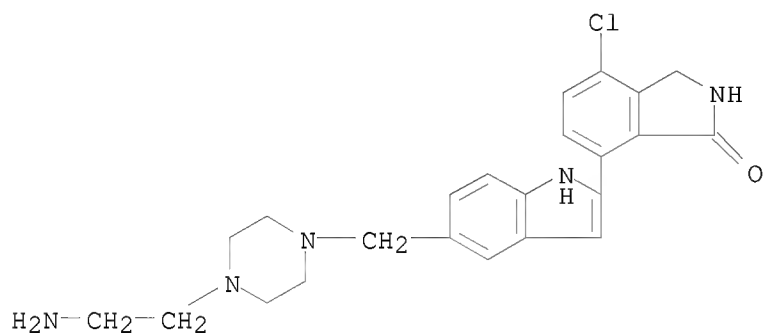
●2 HCl

RN 913385-05-4 CAPLUS
 CN 1H-Isoindol-1-one, 4-(2-furanyl)-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



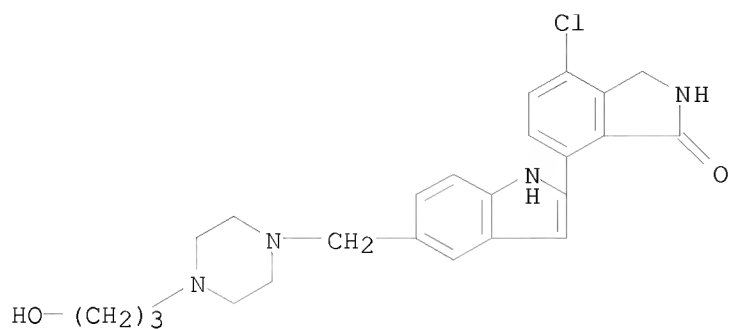
● 2 HCl

RN 913385-45-2 CAPLUS
 CN 1H-Isoindol-1-one, 7-[5-[[4-(2-aminoethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-4-chloro-2,3-dihydro-, hydrochloride (1:3) (CA INDEX NAME)



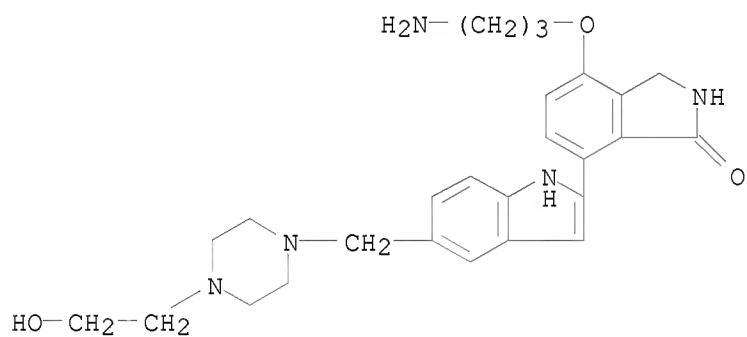
● 3 HCl

RN 913385-46-3 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(3-hydroxypropyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



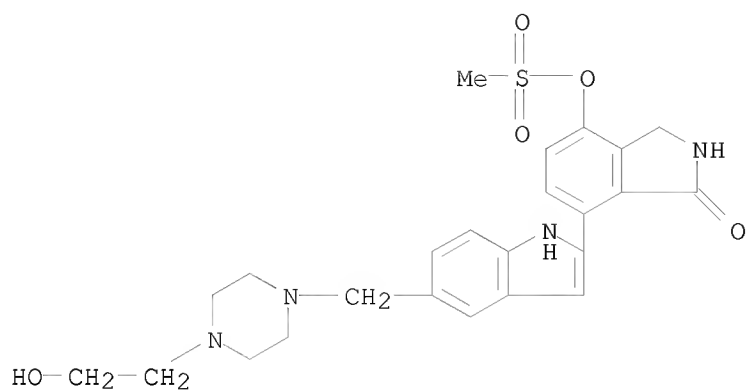
● 2 HCl

RN 913385-77-0 CAPLUS
 CN 1H-Isoindol-1-one, 4-(3-aminopropoxy)-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:3)
 (CA INDEX NAME)



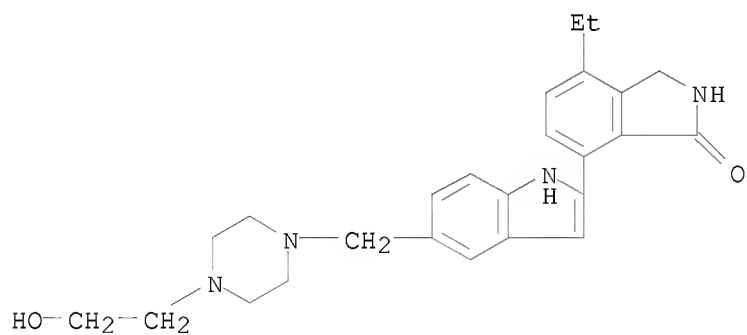
● 3 HCl

RN 913386-46-6 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-4-[(methylsulfonyl)oxy]-, hydrochloride
 (1:2) (CA INDEX NAME)



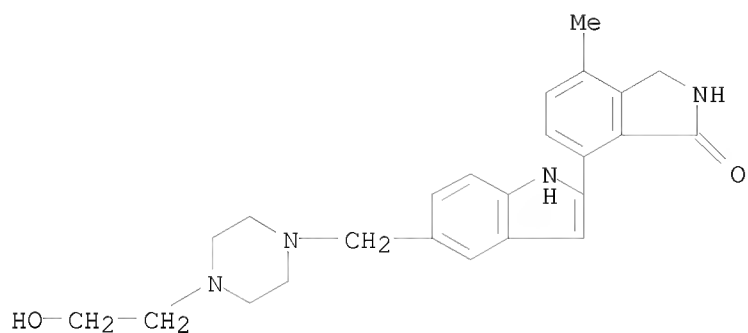
● 2 HCl

RN 913386-59-1 CAPLUS
 CN 1H-Isoindol-1-one, 4-ethyl-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



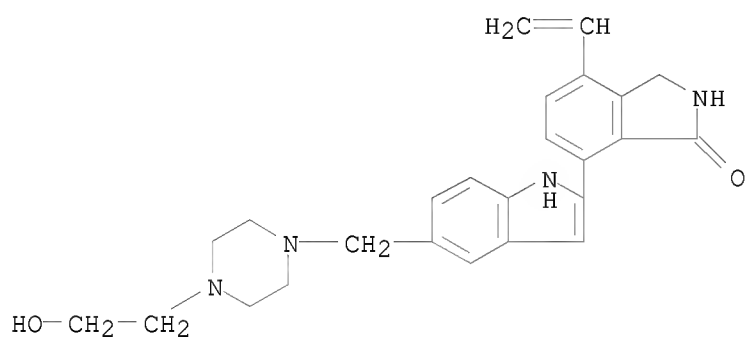
● 2 HCl

RN 913386-60-4 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-4-methyl-, hydrochloride (1:2) (CA INDEX NAME)



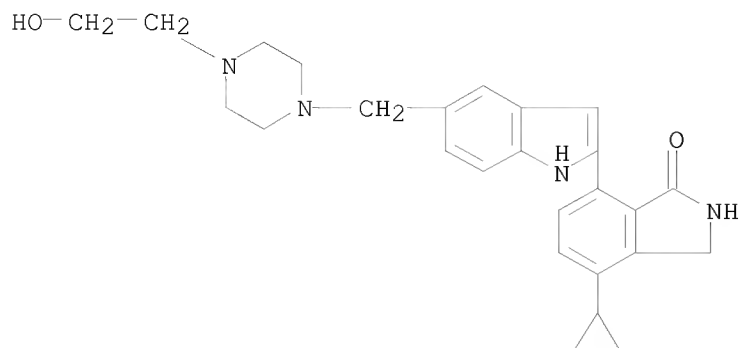
●2 HCl

RN 913386-83-1 CAPLUS
 CN 1H-Isoindol-1-one, 4-ethenyl-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



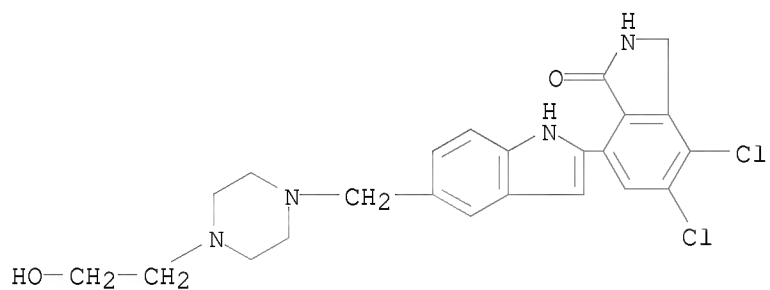
●2 HCl

RN 913386-84-2 CAPLUS
 CN 1H-Isoindol-1-one, 4-cyclopropyl-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



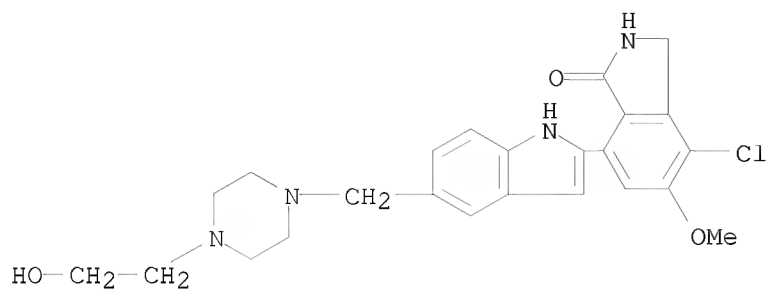
● 2 HCl

RN 913386-96-6 CAPLUS
 CN 1H-Isoindol-1-one, 4,5-dichloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



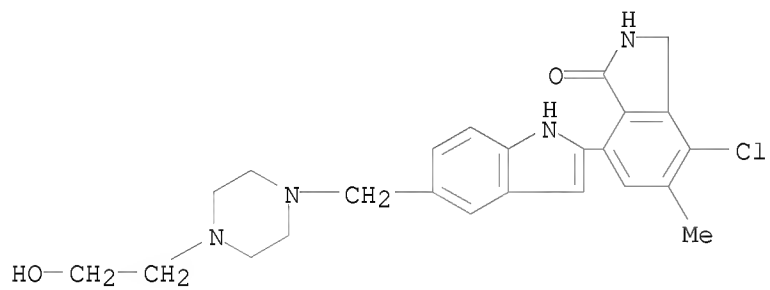
● 2 HCl

RN 913387-00-5 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methoxy-, hydrochloride (1:2) (CA INDEX NAME)



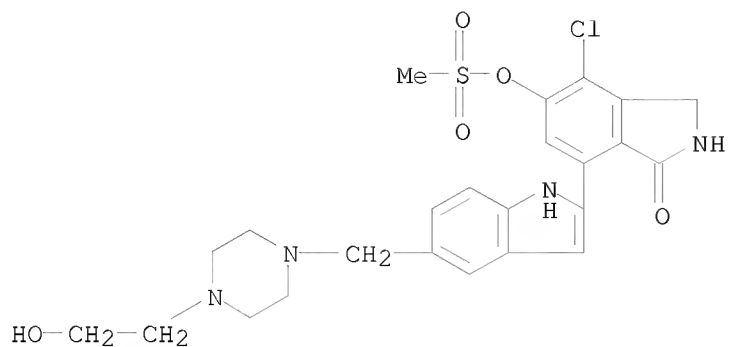
● 2 HCl

RN 913387-02-7 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methyl-, hydrochloride (1:2) (CA INDEX NAME)



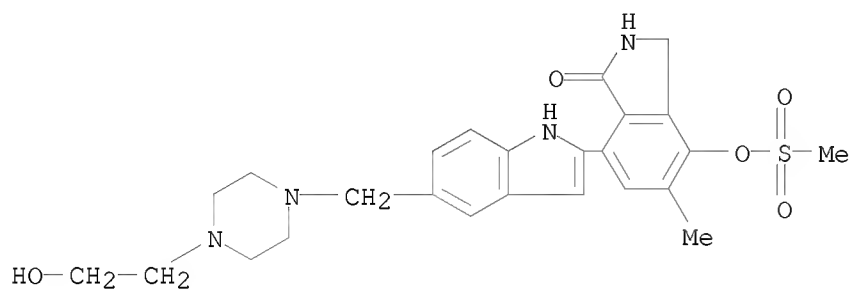
● 2 HCl

RN 913387-07-2 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-[(methylsulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



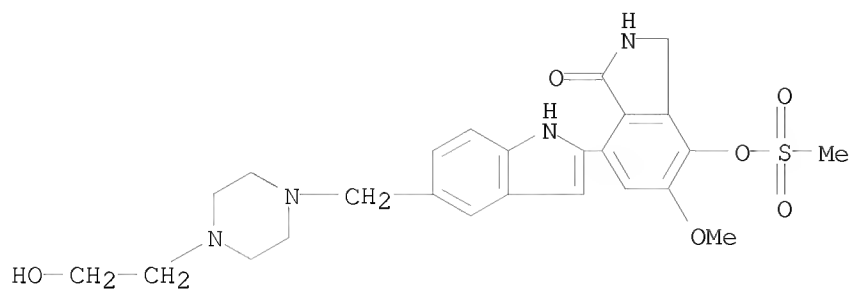
● 2 HCl

RN 913387-13-0 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methyl-4-[(methanesulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



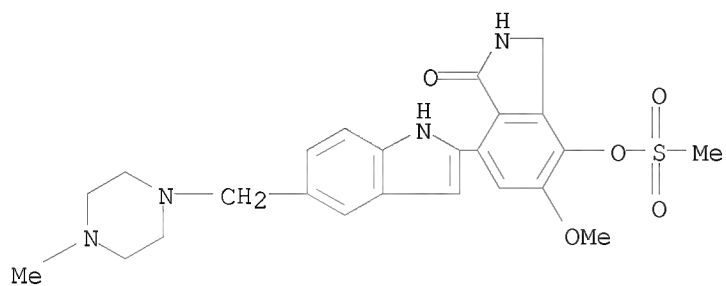
● 2 HCl

RN 913387-18-5 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-5-methoxy-4-[(methanesulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



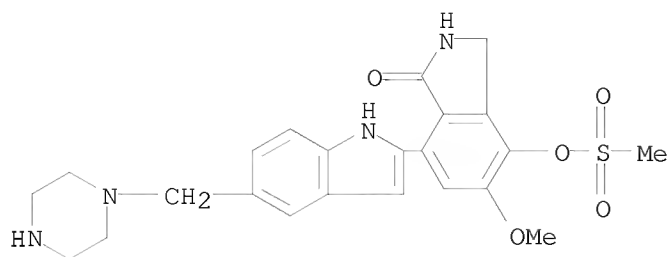
● 2 HCl

RN 913387-25-4 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-5-methoxy-7-[5-[(4-methyl-1-piperazinyl)methyl]-1H-indol-2-yl]-4-[(methylsulfonyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



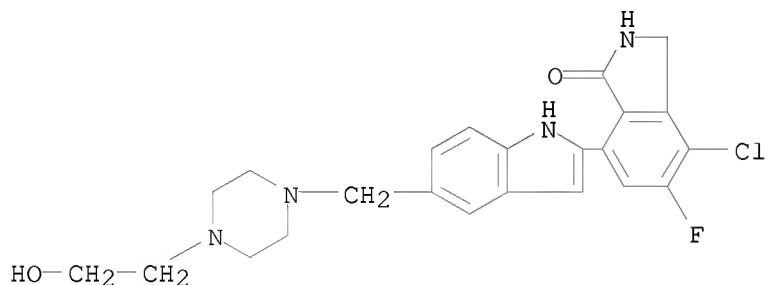
● 2 HCl

RN 913388-09-7 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-5-methoxy-4-[(methylsulfonyl)oxy]-7-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RN 913388-14-4 CAPLUS
 CN 1H-Isoindol-1-one, 4-chloro-5-fluoro-2,3-dihydro-7-[5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:1048545 CAPLUS
 DN 146:45384
 TI Development of 6-substituted indolylquinolinones as potent Chek1 kinase inhibitors
 AU Huang, Shaei; Garbaccio, Robert M.; Fraley, Mark E.; Steen, Justin; Kreatsoulas, Constantine; Hartman, George; Stirdivant, Steve; Drakas, Bob; Rickert, Keith; Walsh, Eileen; Hamilton, Kelly; Buser, Carolyn A.; Hardwick, James; Mao, Xianzhi; Abrams, Marc; Beck, Steve; Tao, Weikang; Lobell, Rob; Sepp-Lorenzino, Laura; Yan, Youwei; Ikuta, Mari; Murphy, Joan Zugay; Sardana, Vinod; Munshi, Sanjeev; Kuo, Lawrence; Reilly, Michael; Mahan, Elizabeth
 CS Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
 SO Bioorganic & Medicinal Chemistry Letters (2006), 16(22), 5907-5912

CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Ltd.

DT Journal

LA English

OS CASREACT 146:45384

AB It was hypothesized that the affinity of the indolylquinolinone series for Chek1 kinase would be improved via C6 substitution into the hydrophobic region I (HI) pocket. An efficient route to 6-bromo-3-indolylquinolinone derivative was developed, and this series was rapidly optimized for potency by modification at C6. A general trend was observed among these low nanomolar Chek1 inhibitors that compds. with multiple basic amines, or elevated polar surface area (PSA) exhibited poor cell potency. Minimization of these parameters (basic amines, PSA) resulted in Chek1 inhibitors with improved cell potency, and preliminary pharmacokinetic data are presented for several of these compds.

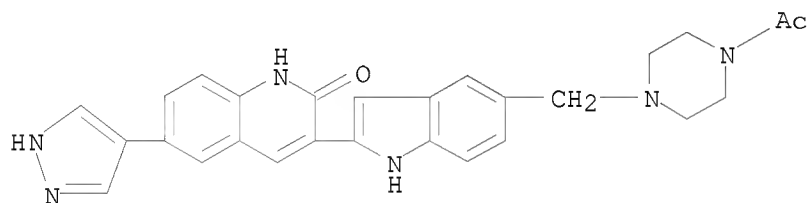
IT 916429-49-7P 916429-50-0P 916429-51-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of 6-substituted indolylquinolinones as potent Chek1 kinase inhibitors)

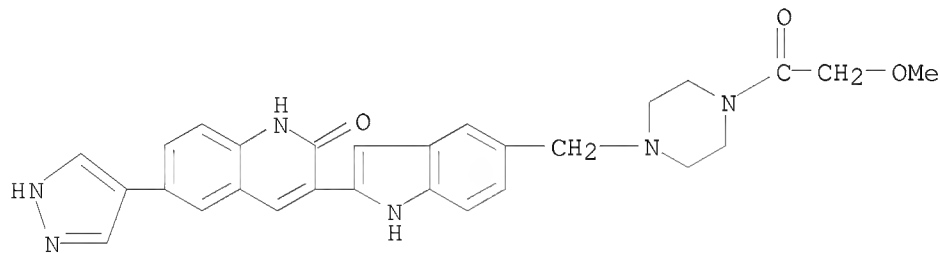
RN 916429-49-7 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(1H-pyrazol-4-yl)- (CA INDEX NAME)



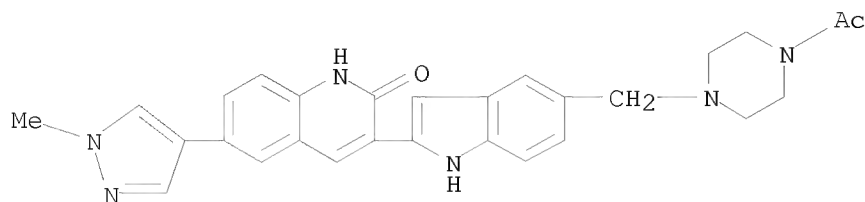
RN 916429-50-0 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(2-methoxyacetyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-6-(1H-pyrazol-4-yl)- (CA INDEX NAME)

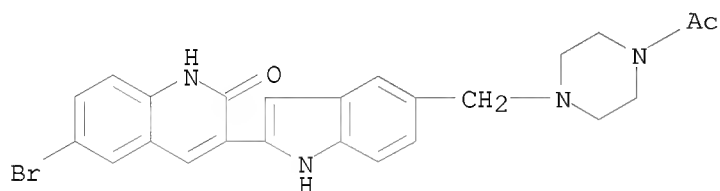


RN 916429-51-1 CAPLUS

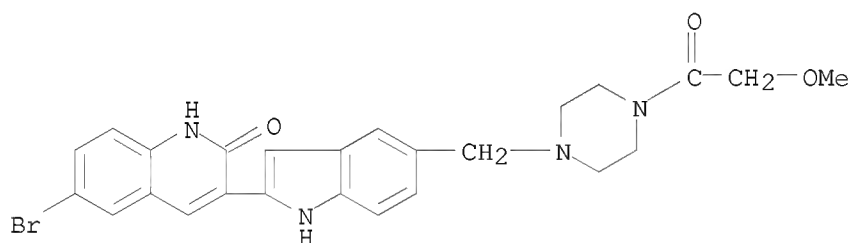
CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-(1-methyl-1H-pyrazol-4-yl)- (CA INDEX NAME)



IT 925688-77-3P 925688-79-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of 6-substituted indolylquinolinones as potent Chek1 kinase
 inhibitors)
 RN 925688-77-3 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-6-
 bromo- (CA INDEX NAME)



RN 925688-79-5 CAPLUS
 CN 2(1H)-Quinolinone, 6-bromo-3-[5-[[4-(2-methoxyacetyl)-1-
 piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

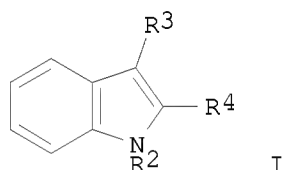


RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:437069 CAPLUS
 DN 144:468020
 TI Process for preparation of 2-substituted indoles from dihalovinylanilines
 and organoboron reagents.
 IN Lautens, Mark; Fang, Yuanqing
 PA Can.
 SO PCT Int. Appl., 172 pp.
 CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2006047888 | A1 | 20060511 | WO 2005-CA1703 | 20051104 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | CA 2586910 | A1 | 20060511 | CA 2005-2586910 | 20051104 |
| | EP 1817283 | A1 | 20070815 | EP 2005-803043 | 20051104 |
| | R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| | US 20080039625 | A1 | 20080214 | US 2007-718769 | 20070924 |
| PRAI | US 2004-625102P | P | 20041105 | | |
| | US 2005-662797P | P | 20050318 | | |
| | WO 2005-CA1703 | W | 20051104 | | |
| OS | MARPAT 144:468020 | | | | |
| GI | | | | | |



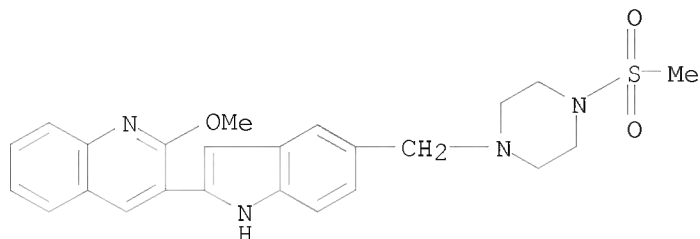
AB Title compds. [I; R2 = H, (substituted) alkyl, cycloalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R3 = H, (substituted) alkyl, haloalkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, aralkyl, heteroaralkyl; R4 = (substituted) mono- or polycyclic aryl, heteroaryl, alkyl, alkenyl bonded to the 2-position of the indole ring via a C-C bond] were prepared by reaction of ortho-dihalovinylanilines (II; X = Br, Cl, iodo; R2, R3 as above) with boronic esters, boronic acids, boronic acid anhydrides, trialkylboranes, or 9-BBN derivs. of R4 in the presence of base, Pd metal precatalyst, and a ligand. Thus, 2-(2,2-dibromovinyl)phenylamine, PhB(OH)2, K3PO4.H2O, Pd(OAc)2, and s-Phos were heated in PhMe at 90° for 6 h to give 84% 2-phenylindole.

IT 796854-61-0P

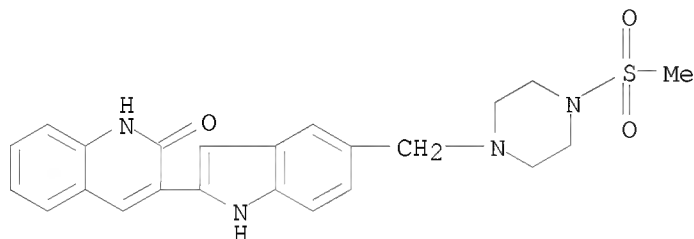
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for preparation of substituted indoles from dihalovinylanilines and organoboron reagents)

RN 796854-61-0 CAPLUS
 CN Quinoline, 2-methoxy-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



IT 335649-90-6P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (process for preparation of substituted indoles from dihalovinylanilines and organoboron reagents)
 RN 335649-90-6 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2006:95834 CAPLUS
 DN 145:292393
 TI Applying statistical design of experiments and automation to the rapid optimization of metal-catalyzed processes in process development
 AU McWilliams, J. Christopher; Sidler, D. Richard; Sun, Yongkui; Mathre, David J.
 CS Department of Process Research, Merck & Co., Rahway, NJ, USA
 SO JALA (2005), 10(6), 394-407
 CODEN: JALLFO; ISSN: 1535-5535
 PB Elsevier Inc.
 DT Journal
 LA English
 OS CASREACT 145:292393
 AB The application of automation in conjunction with DoE (design of expts.) designs towards the rapid discovery and optimization of metal-catalyzed reactions used in the synthetic preparation of clin. drug candidates at Merck

Process Research is demonstrated with three examples. A description of the software and hardware is provided, followed by three examples highlighting these applications. The first example highlights a DoE optimization of a platinum-catalyzed chemoselective hydrogenation of a nitroarom. nitrile. In the second example, automated screening is employed to discover a highly efficient palladium catalyst that affects nitrostyrene cyclization under a carbon monoxide reducing atmosphere. In the last example, a rapid discovery and DoE optimization of a rhodium-catalyzed diastereoselective hydrogenation of an unsatd. ester is detailed.

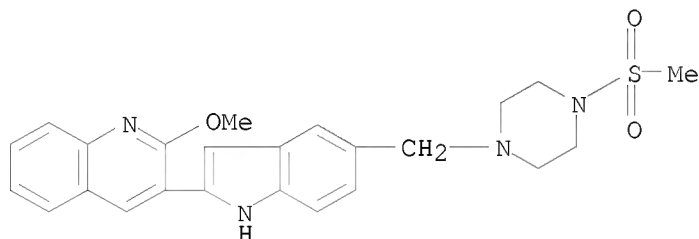
IT 796854-61-0P

RL: IMF (Industrial manufacture); PREP (Preparation)

(Applying statistical design of expts. and automation to the rapid optimization of metal-catalyzed processes in process development)

RN 796854-61-0 CAPLUS

CN Quinoline, 2-methoxy-3-[5-[[4-(methanesulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:571929 CAPLUS

DN 143:298428

TI Induction of CYP1A in the beagle dog by an inhibitor of kinase insert domain-containing receptor: Differential effects in vitro and in vivo on mRNA and functional activity

AU Gibson, Christopher R.; Lin, Charles; Singh, Rominder; Brown, Cheri M.; Richards, Karen; Brunner, Janice; Michel, Kimberly; Adelsberger, Jennifer; Carlini, Edward; Boothe-Genthe, Catherine; Raab, Conrad; Luu, Minh; Michael, Aimee; Parikh, Mona; Ciecko, Patrice; Subramanian, Raju; Krolikowski, Paul; Rodrigues, A. David; Baillie, Thomas A.; Rushmore, Thomas H.

CS Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, USA

SO Drug Metabolism and Disposition (2005), 33(7), 1044-1051
CODEN: DMDSAI; ISSN: 0090-9556

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AB Compound I [3-[5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one] is a potent inhibitor of human kinase insert domain-containing receptor (KDR kinase), which is under investigation for the treatment of cancer. Bile duct-cannulated male beagle dogs were administered 6 mg/kg compound I q.d. for 14 days. There was an approx. 2.5-fold decrease in the

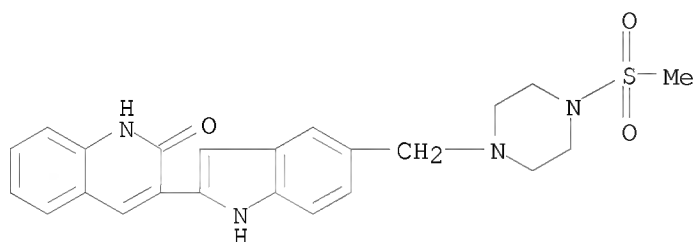
mean plasma area under the curve of I on days 7 and 14 (.apprx.11.3 $\mu\text{M} \cdot \text{h}$), relative to day 1 (28.2 $\mu\text{M} \cdot \text{h}$). In the dog, compound I was eliminated by metabolism, with a major pathway being aromatic hydroxylation and subsequent sulfation to form the metabolite M3. Metabolic profiling suggested that the pathway leading to the formation of the sulfated conjugate M3 was induced upon multiple dosing of I. Studies conducted in vitro suggested that CYP1A1/2 was responsible for the formation of the hydroxylated metabolite, which is sulfated to yield M3. Addnl. studies confirmed induction of CYP1A protein and activity in the livers of dogs treated with I. However, studies in a dog hepatocyte model of induction showed a surprising decrease both in CYP1A mRNA and enzymic activity in the presence of I, emphasizing the need to consider the results from a variety of in vitro and in vivo studies in deriving an understanding of the metabolic fate of a drug candidate. It is concluded that the autoinduction observed after multiple treatments with compound I occurs since compound I is both an inducer and a substrate for dog CYP1A.

IT 335649-90-6D, oxygenated 335649-91-7 864852-18-6
864852-20-0 864852-22-2 864852-29-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CYP1A activity and mechanism of kinase insert domain-containing receptor inhibitors pharmacokinetics in dog)

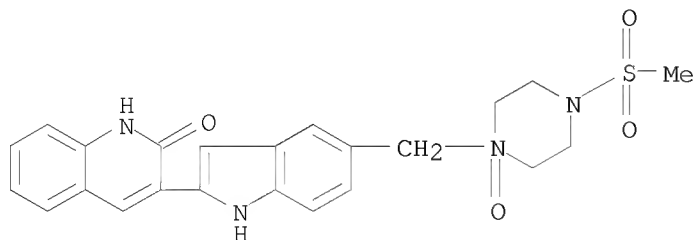
RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



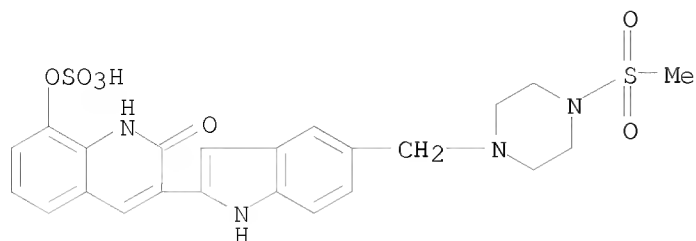
RN 335649-91-7 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-oxido-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



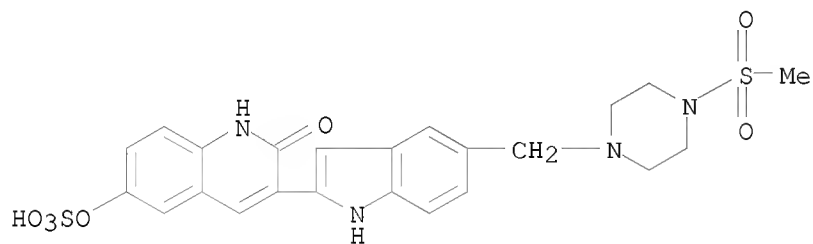
RN 864852-18-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-8-(sulfooxy)- (CA INDEX NAME)



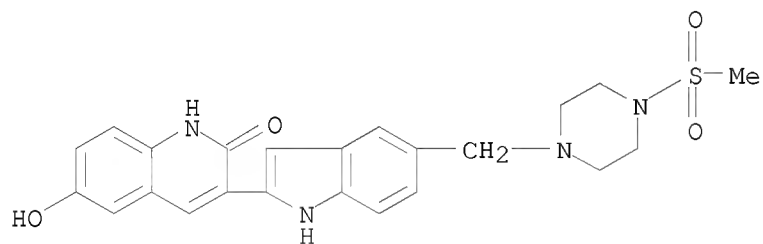
RN 864852-20-0 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methanesulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-6-(sulfoxy)- (CA INDEX NAME)



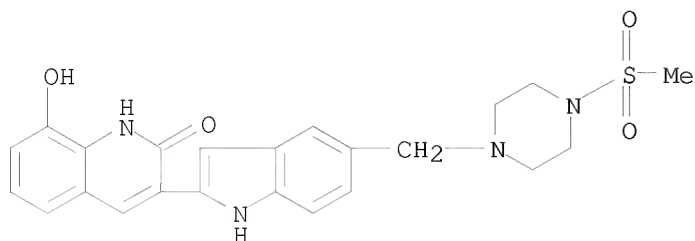
RN 864852-22-2 CAPLUS

CN 2(1H)-Quinolinone, 6-hydroxy-3-[5-[[4-(methanesulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

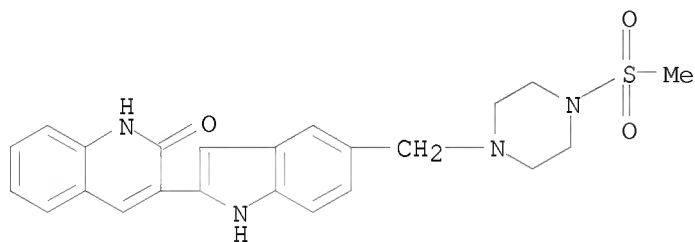


RN 864852-29-9 CAPLUS

CN 2(1H)-Quinolinone, 8-hydroxy-3-[5-[[4-(methanesulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



IT 335649-90-6, [3-[5-(4-Methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one]
 RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (CYP1A activity and mechanism of kinase insert domain-containing receptor inhibitors pharmacokinetics in dog)
 RN 335649-90-6 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:510364 CAPLUS
 DN 143:193876
 TI A highly active catalyst for the reductive cyclization of ortho-nitrostyrenes under mild conditions
 AU Davies, Ian W.; Smitrovich, Jacqueline H.; Sidler, Rick; Qu, Chuanxing; Gresham, Venita; Bazaral, Charles
 CS Department of Process Research, Merck & Co., Inc., Rahway, NJ, 07065-0900, USA
 SO Tetrahedron (2005), 61(26), 6425-6437
 CODEN: TETRAB; ISSN: 0040-4020
 PB Elsevier B.V.
 DT Journal
 LA English
 OS CASREACT 143:193876
 AB A mild and efficient method for the palladium-catalyzed reductive cyclization of ortho-nitrostyrenes to afford indoles is reported. Treatment of ortho-nitrostyrenes with 0.1 mol% palladium (II) trifluoroacetate [Pd(TFA)2] and 0.7 mol% 3,4,7,8-tetramethyl-1,10-phenanthroline (tm-phen) in DMF at 15 psig CO and 80 °C afforded

indoles in good to excellent yields. When the reaction was conducted in toluene, the corresponding N-hydroxyindole was isolated. A mechanism that accounts for the formation of N-hydroxyindole is proposed.

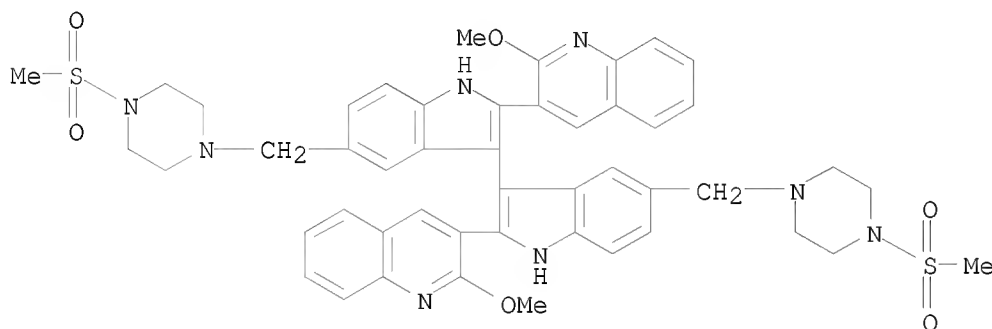
IT 850171-43-6P

RL: BYP (Byproduct); PREP (Preparation)

(byproduct from the preparation of indoles via palladium-catalyzed reductive cyclization of ortho-nitrostyrenes)

RN 850171-43-6 CAPLUS

CN Piperazine, 1,1'-[[2,2'-bis(2-methoxy-3-quinolinyl)[3,3'-bi-1H-indole]-5,5'-diyl]bis(methylene)]bis[4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



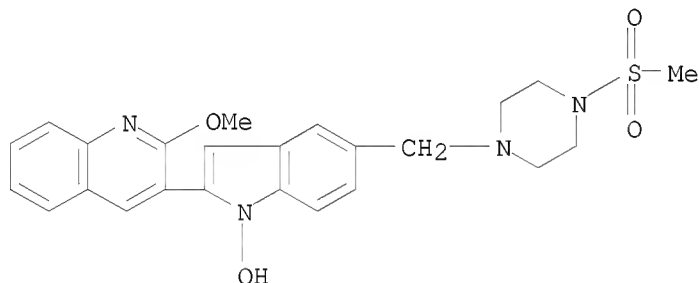
IT 796854-64-3P

RL: CPN (Combinatorial preparation); CMBI (Combinatorial study); PREP (Preparation)

(preparation of indoles via palladium-catalyzed reductive cyclization of ortho-nitrostyrenes using either non-parallel or parallel synthesis)

RN 796854-64-3 CAPLUS

CN Quinoline, 3-[1-hydroxy-5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-2-methoxy- (CA INDEX NAME)



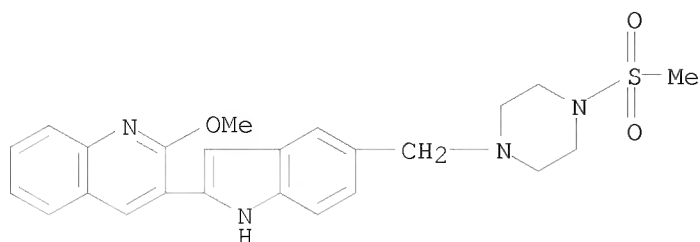
IT 796854-61-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of indoles via palladium-catalyzed reductive cyclization of ortho-nitrostyrenes using either non-parallel or parallel synthesis)

RN 796854-61-0 CAPLUS

CN Quinoline, 2-methoxy-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:174313 CAPLUS
DN 142:309130
TI Concerns in the development of an assay for determination of a highly conjugated adsorption-prone compound in human urine
AU Xu, Yang; Du, Lihong; Rose, Mark J.; Fu, Irong; Woolf, Eric J.; Musson, Donald G.
CS Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2005), 818(2), 241-248
CODEN: JCBAAI; ISSN: 1570-0232
PB Elsevier B.V.
DT Journal
LA English
AB Concerns in pre-anal. handling of urine samples are discussed using a new KDR kinase inhibitor, 3-[5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one (compound A), as an example of a case where high light sensitivity and low analyte recovery (high affinity for container surface) were found. The absence of these problems in plasma samples may be a result of the plasma protein content. Low recovery of the analyte from urine can be remedied by either changing the container or by using additives, such as bovine serum albumin (BSA) or non-ionic surfactant Tween-20. In the case of compound A, changing containers (polypropylene vs. glass vial) or addition of BSA did bring analyte recovery up to 80%. However, the addition of 0.2% Tween-20 into urine quality controls (QCs) gave more than 95% analyte recovery, indicating effective reduction of analyte loss to the surface of containers. The urine assay using mixed-mode SPE and LC-MS/MS was not affected significantly by introducing Tween-20 into the samples. The mean SPE extraction recovery was 68.4% and matrix suppression of ionization on MS was less than 8% at all analyte concns. The linear range of the calibration curve was 0.5-400 ng/mL on PE Sciex API 3000 LC-MS/MS system. The assay intraday accuracy and precision were 92.1-104.8% and <4.2% (%CV), resp. Urine QC samples, containing 0.2% Tween-20, gave excellent recovery after three cycles of freeze and thaw. Since analyte loss to its urine container surface is not unique to compound A (M. Schwartz, W. Kline, B. Matuszewski, Anal. Chim. Acta 352 (1997) 299-307; A. L. Fisher, E. DePuy, T. Shih, R. Stearns, Y. Lee, K. Gottesdiener, S. Flattery, M. De Smet, B. Keymeulen, D. G. Musson, J. Pharm. Biomed. Anal. 26 (2001) 739-752), we suggest an evaluation of the potential problem in the early stages of urine assay development to ensure reliable quantitation of analytes. The addition of Tween-20 can serve as a useful anal. tool to other analytes with similar situations.
IT 335649-90-6, 3-[5-(4-Methanesulfonyl-piperazin-1-ylmethyl)-1H-

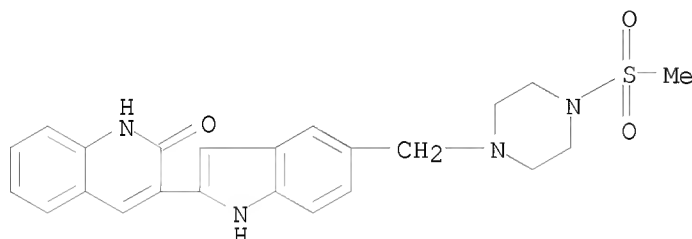
indol-2-yl]-1H-quinolin-2-one

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(concerns in development of an assay for determination of highly conjugated adsorption-prone compound in human urine)

RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:172057 CAPLUS

DN 142:411180

TI Synthesis of 5-Substituted-1H-indol-2-yl-1H-quinolin-2-ones: A Novel Class of KDR Kinase Inhibitors

AU Kuethe, Jeffrey T.; Wong, Audrey; Qu, Chuanxing; Smitrovich, Jacqueline; Davies, Ian W.; Hughes, David L.

CS Department of Process Research, Merck & Co., Inc., Rahway, NJ, 07065, USA

SO Journal of Organic Chemistry (2005), 70(7), 2555-2567

CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

OS CASREACT 142:411180

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A number of approaches for the synthesis of the 1H-indol-2-yl-1H-quinolin-2-one ring system found in the potent and selective KDR kinase inhibitor I are described. The preparation and reaction of trimethylsilylnitrobenzene II with 2-methoxy-3-quinolinecarboxaldehyde afforded alc. III, which was the key intermediate for the preparation of the target compds. Conversion of alc. III to either nitroketone IV or nitrostyrene V set the stage for reductive cyclization. The quinolin-2-one functionality was unmasked in the last step to provide compound I in 56-60% overall yield from readily available starting materials.

IT 850171-43-6P

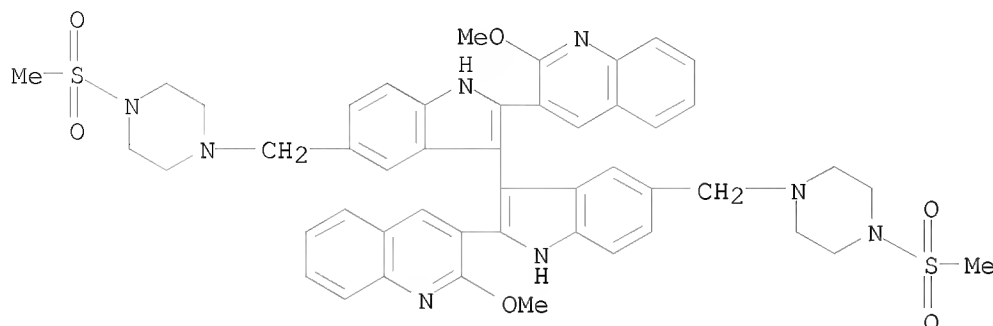
RL: BYP (Byproduct); PREP (Preparation)

(synthesis of 5-substituted 1H-indol-2-yl-1H-quinolin-2-ones via

Fischer-indole cyclization, Pd-catalyzed annulation, and by reductive cyclization of nitro ketone or nitro styrene derivs.)

RN 850171-43-6 CAPLUS

CN Piperazine, 1,1'-[[2,2'-bis(2-methoxy-3-quinolinyl)[3,3'-bi-1H-indole]-5,5'-diyl]bis(methylene)]bis[4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



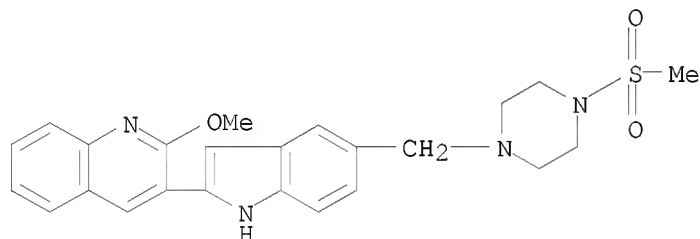
IT 796854-61-0P 850171-34-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of 5-substituted 1H-indol-2-yl-1H-quinolin-2-ones via Fischer-indole cyclization, Pd-catalyzed annulation, and by reductive cyclization of nitro ketone or nitro styrene derivs.)

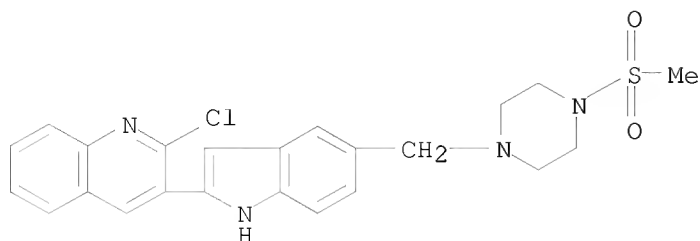
RN 796854-61-0 CAPLUS

CN Quinoline, 2-methoxy-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

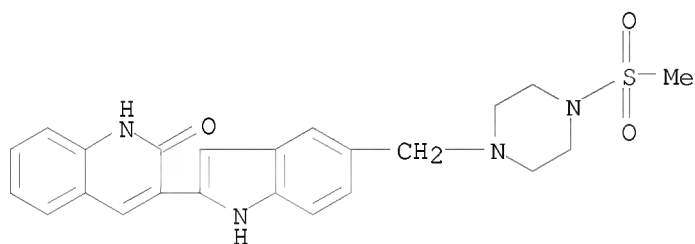


RN 850171-34-5 CAPLUS

CN Quinoline, 2-chloro-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

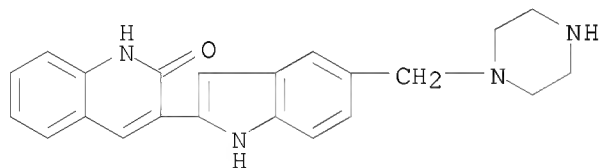


IT 415684-58-1P 771477-43-1P 850171-36-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (synthesis of 5-substituted 1H-indol-2-yl-1H-quinolin-2-ones via
 Fischer-indole cyclization, Pd-catalyzed annulation, and by reductive
 cyclization of nitro ketone or nitro styrene derivs.)
 RN 415684-58-1 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-
 indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)



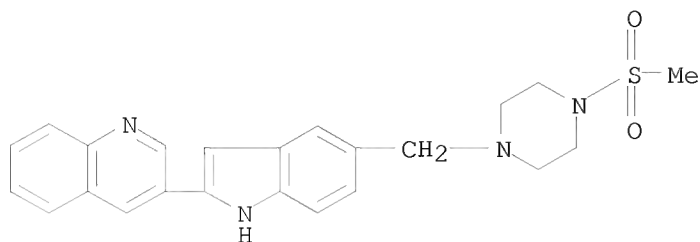
● HCl

RN 771477-43-1 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-,
 hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

RN 850171-36-7 CAPLUS
 CN Quinoline, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-
 (CA INDEX NAME)



RE.CNT 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:85916 CAPLUS

DN 142:328833

TI Simultaneous determination of a novel KDR kinase inhibitor and its N-oxide metabolite in human plasma using 96-well solid-phase extraction and liquid chromatography/tandem mass spectrometry

AU Xu, Yang; Du, Lihong; Soli, Eric D.; Braun, Matthew P.; Dean, Dennis C.; Musson, Donald G.

CS Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, 19486, USA

SO Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2005), 817(2), 287-296

CODEN: JCBAAI; ISSN: 1570-0232

PB Elsevier B.V.

DT Journal

LA English

AB To support pharmacokinetic studies, a selective and sensitive liquid chromatog./tandem mass spectrometry (LC-MS/MS) method was developed and validated for the simultaneous determination of a novel KDR kinase inhibitor

(1) and its active metabolite (2) in human plasma. The method is fully automated using a Packard MultiPROBE II system and a TomTec Quadra 96 liquid handling workstation to perform sample preparation and solid-phase extraction (SPE).

Following the extraction on a mixed-mode SPE using Oasis MCX 96-well plate, the analytes were separated on a Aquasil C18 column (50 mm + 2.1 mm, i.d., 3 µm) with a mobile phase consisting of acetonitrile/ammonium acetate buffer (5 mM, pH 5.0) (60/40, volume/volume). The run time for each injection was 4.5 min with the retention times of approx. 2.0 and 2.7 min for 1 and 2 resp., at a flow rate of 0.25 mL/min. A tandem mass spectrometric detection was conducted using multiple reaction monitoring (MRM) under the pos. ion mode with a turbo ion-spray interface. The linear ranges of the calibration curves were 0.05-400 ng/mL for 1 and 0.1-400 ng/mL for 2 on a PE Sciex API 4000 LC-MS/MS system. The lower limits of quantitation (LLOQ) of the assay were 0.05 and 0.1 ng/mL for 1 and 2 resp., when 0.4 mL of plasma was processed. Intra-day assay precision (using 5 standard curves prepared by spiking compds. to 5 lots of plasma) was < 4.9% for 1 and < 9.6% for 2 on each concentration. Assay accuracy was found to be 95.1-104.6% of nominal for 1 stds. and 93.5-105.6% for 2 stds. QC samples were stable when kept at room temperature for 4 h, at -70 °C for 10 days, and after 3 freeze-thaw cycles. The extraction recoveries were 80, 83, and 84% for 1 and 2

and I.S. resp., and no significant matrix effects were observed. The method was successfully applied to plasma samples from clin. studies after oral administration of compound 1.

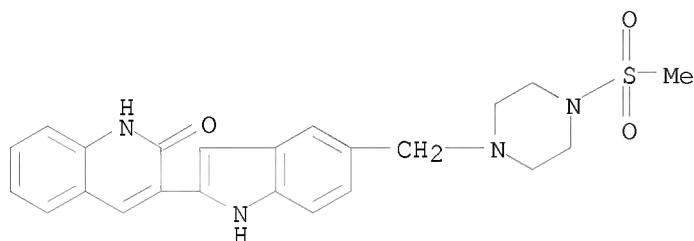
IT 335649-90-6 335649-91-7

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(simultaneous determination of novel KDR kinase inhibitor and its N-oxide metabolite in human plasma by LC-MS/MS)

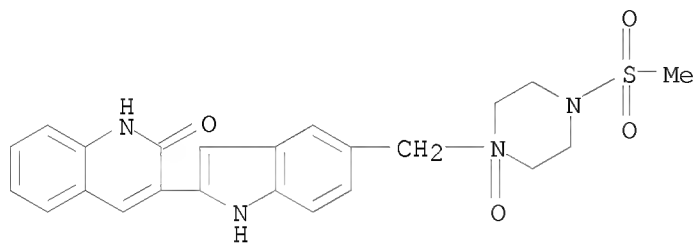
RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 335649-91-7 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-oxido-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:14366 CAPLUS

DN 142:113888

TI Substituted indoles and a process for their preparation via
Pd/diamine-catalyzed reductive cyclization of ortho-nitrostyrenes under CO
pressure

IN Davies, Ian W.; Smitrovich, Jacqueline H.; Qu, Chuanxing

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.

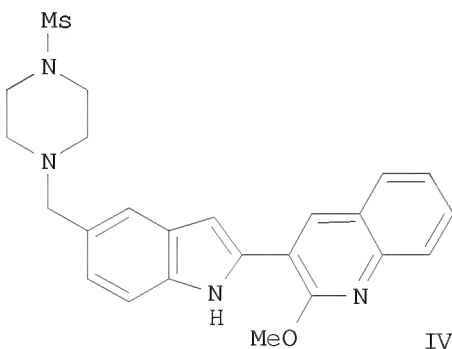
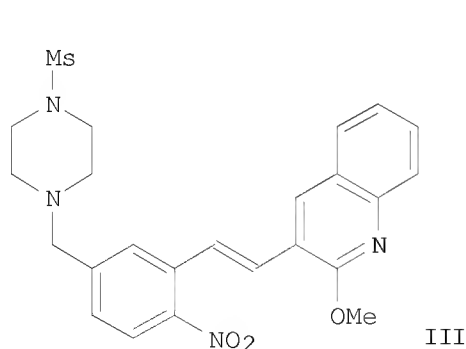
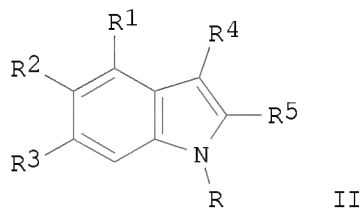
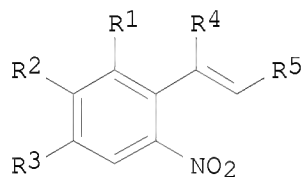
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APPLICATION NO.

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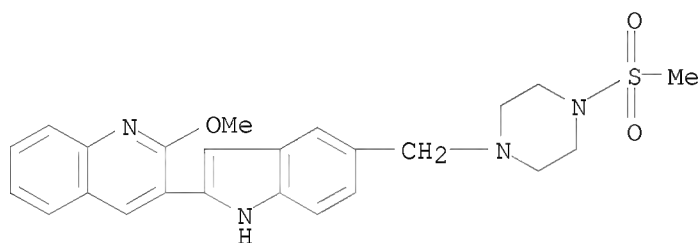
| | | | | | |
|------|--|----|----------|------------------|----------|
| PI | WO 2005000804 | A2 | 20050106 | WO 2004-US17357 | 20040601 |
| | WO 2005000804 | A3 | 20050804 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2004251175 | A1 | 20050106 | AU 2004-251175 | 20040601 |
| | CA 2526988 | A1 | 20050106 | CA 2004-2526988 | 20040601 |
| | EP 1633694 | A2 | 20060315 | EP 2004-776226 | 20040601 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| | CN 1798726 | A | 20060705 | CN 2004-80015534 | 20040601 |
| | JP 2006526654 | T | 20061124 | JP 2006-515094 | 20040601 |
| | US 20070054921 | A1 | 20070308 | US 2005-557537 | 20051121 |
| | IN 2005DN05638 | A | 20080201 | IN 2005-DN5638 | 20051205 |
| PRAI | US 2003-476089P | P | 20030605 | | |
| | WO 2004-US17357 | W | 20040601 | | |
| OS | CASREACT 142:113888; MARPAT 142:113888 | | | | |
| GI | | | | | |



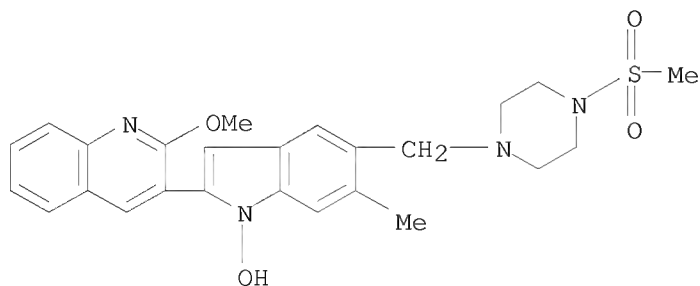
AB The invention is directed to novel compds. I and II as well as a process for the preparation of II from I, via palladium-catalyzed reductive cyclization

of I under CO pressure with aromatic diamines as ligands, wherein R1 = H, (un)substituted alkyl or alkoxy; R2 = H, (un)substituted alkyl, alkoxy or halo; R3 = H, (un)substituted alkyl or alkoxy; R2 and R3 can link together; R4 = H, (un)substituted alkyl, alkoxy or ester; R5 = (un)substituted alk(en/yn)yl, (hetero)aryl, amide or ketone; R = H or OH; or salts thereof. For example, An autoclave was charged with III (15 g, preparation given), Pd(OTf)₂ (0.020 g), 3,4,7,8-tetramethyl-1,10-phenanthroline (0.102 g) and DMF (100 mL). After the vessel was purged three times successively with N₂ and CO, the reactor was pressurized to 15 psig with CO and aged at 70 °C for 14 h. IV was isolated in 83 % yield after work-up. The new process can be conducted under milder conditions, such as lower temperature and CO pressure, as well as lower catalyst and ligand loading, which simplify purification II are useful intermediates of pharmaceutical compds., such as KDR inhibitors and GNRH inhibitors (no data).

IT 796854-61-0P, 2-Methoxy-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]quinoline 820976-93-0P,
2-(2-Methoxyquinolin-3-yl)-6-methyl-5-[[4-(methylsulfonyl)piperazin-1-yl]methyl]-1H-indol-1-ol
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(target; preparation of indoles via Pd/diamine-catalyzed reductive cyclization of ortho-nitrostyrenes under CO pressure)
RN 796854-61-0 CAPLUS
CN Quinoline, 2-methoxy-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 820976-93-0 CAPLUS
CN Quinoline, 3-[1-hydroxy-6-methyl-5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-2-methoxy- (CA INDEX NAME)



IT 335649-90-6P 820977-27-3P, 2-Methoxy-3-[5-(piperazin-1-

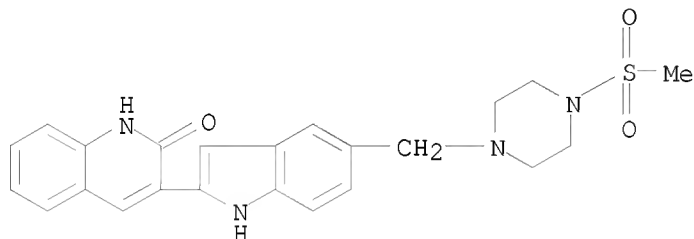
ylmethyl)-1H-indol-2-yl]quinoline

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(target; preparation of indoles via Pd/diamine-catalyzed reductive cyclization of ortho-nitrostyrenes under CO pressure)

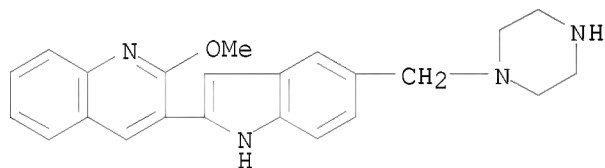
RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 820977-27-3 CAPLUS

CN Quinoline, 2-methoxy-3-[5-(1-piperazinylmethyl)-1H-indol-2-yl]- (CA INDEX NAME)



L6 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1005650 CAPLUS

DN 142:134559

TI A Concise Synthesis of a Novel Antiangiogenic Tyrosine Kinase Inhibitor

AU Payack, Joseph F.; Vazquez, Enrique; Matty, Louis; Kress, Michael H.; McNamara, James

CS Department of Process Research, Merck & Co. Inc., Rahway, NJ, 07065-0900, USA

SO Journal of Organic Chemistry (2005), 70(1), 175-178

CODEN: JOCEAH; ISSN: 0022-3263

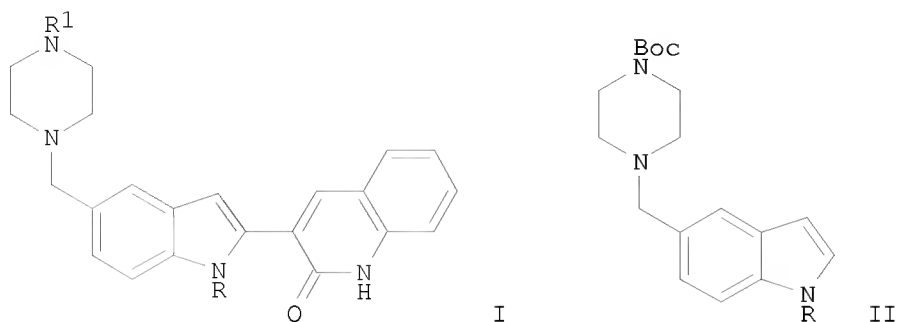
PB American Chemical Society

DT Journal

LA English

OS CASREACT 142:134559

GI



AB Antiangiogenic compound I (R = H; R1 = MeSO2) (an inhibitor of the endothelial VEGF receptor KDR) is prepared concisely and efficiently on kilogram scale using the Suzuki-Miyaura coupling of a boronic acid generated in situ from Boc-protected indolemethylpiperazine II (Boc = Me3COCO) with 3-bromoquinolin-2-one as the key step. 5-Cyanoindole is Boc protected at the indole nitrogen, reduced to the aldehyde with DIBAL, and reductively aminated with Boc-piperazine using sodium triacetoxyborohydride to yield II. Methyltrioxorhenium-mediated oxidation of 3-bromoquinoline followed by rearrangement of the N-oxide with p-toluenesulfonyl chloride yields 3-bromoquinolin-2-one. Lithiation of II with LDA at <5° followed by addition of triisopropyl borate and quenching with hydrochloric acid yields a 2-indoleboronic acid which is coupled with 3-bromoquinolin-2-one in the presence of palladium acetate, triphenylphosphine, and dicyclohexylamine to yield I (R = R1 = Boc) in 88% yield. Cleavage of the Boc groups with hydrochloric acid followed by mesylation of the piperazine yields I (R = H; R1 = MeSO2).

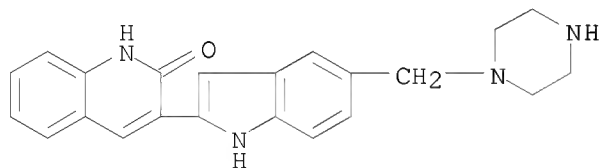
IT 771477-43-1P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(concise preparation of an antiangiogenic compound on kilogram scale using a Suzuki-Miyaura coupling of an indoleboronic acid (generated in situ) and a bromoquinolinone as the key step)

RN 771477-43-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



● 2 HCl

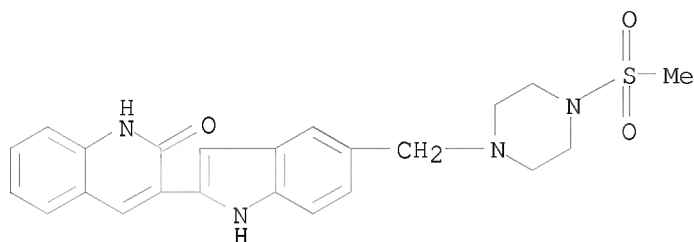
IT 335649-90-6P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(concise preparation of an antiangiogenic compound on kilogram scale using a Suzuki-Miyaura coupling of an indoleboronic acid (generated in situ) and a bromoquinolinone as the key step)

RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:857555 CAPLUS

DN 141:337784

TI Formulations for tyrosine kinase inhibitors

IN Karki, Shyam B.; Deshpande, Sameer R.; Thompson, Karen C.; Payne, Anne H.; Gande, Thomas P.

PA Merck & Co. Inc., USA

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|------------------|----------|
| PI | WO 2004087651 | A2 | 20041014 | WO 2004-US8828 | 20040323 |
| | WO 2004087651 | A3 | 20041216 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | AU 2004225949 | A1 | 20041014 | AU 2004-225949 | 20040323 |
| | AU 2004225949 | B2 | 20061102 | | |
| | CA 2519106 | A1 | 20041014 | CA 2004-2519106 | 20040323 |
| | EP 1610614 | A2 | 20060104 | EP 2004-758216 | 20040323 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | |
| | CN 1764381 | A | 20060426 | CN 2004-80007813 | 20040323 |
| | JP 2006521360 | T | 20060921 | JP 2006-507476 | 20040323 |

| | | | | | |
|------|-----------------|----|----------|----------------|----------|
| | US 20060093666 | A1 | 20060504 | US 2005-544213 | 20050802 |
| | IN 2005DN04097 | A | 20070831 | IN 2005-DN4097 | 20050912 |
| PRAI | US 2003-458094P | P | 20030327 | | |
| | WO 2004-US8828 | A | 20040323 | | |

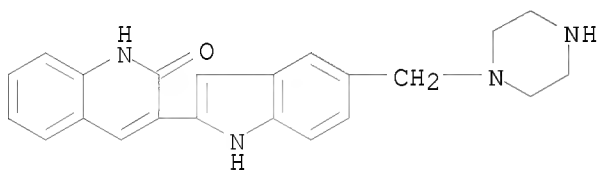
AB The present invention is related to a powder, powder blend or granulation formulation of 3-[5-(4-methanesulfonylpiperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one (I), a tyrosine kinase inhibitor, which is adapted for reconstitution with a diluent. This invention is also related to an aqueous suspension, or a dispersion, particularly to a stable oral pharmaceutical formulation, comprising granules of I mixed with a diluent. Thus, a formulation contained I 1080.0, Avicel PH101 800.0, lactose 1860.0, Klucel EXF 120.0, AcDiSol 120.0, and Mg stearate 20.0 mg/bottle.

IT 771477-43-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(formulations for tyrosine kinase inhibitors)

RN 771477-43-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-(1-piperazinylmethyl)-1H-indol-2-yl]-, hydrochloride (1:2) (CA INDEX NAME)



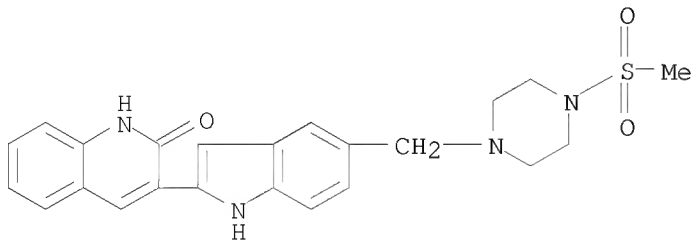
● 2 HCl

IT 335649-90-6P 415684-58-1P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(formulations for tyrosine kinase inhibitors)

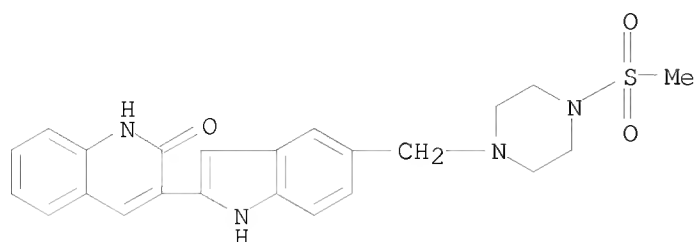
RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



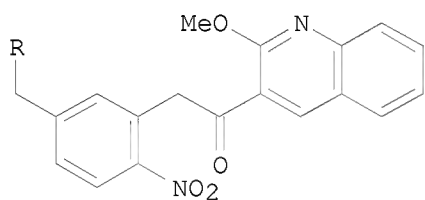
RN 415684-58-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)

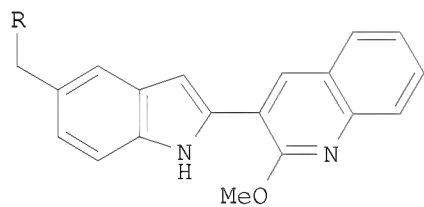


● HCl

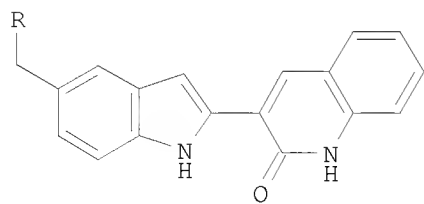
L6 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:804130 CAPLUS
 DN 141:424102
 TI Synthesis of Novel KDR Kinase Inhibitors through Catalytic Reductive
 Cyclization of o-Nitrobenzylcarbonyl Compounds
 AU Wong, Audrey; Kuethe, Jeffrey T.; Davies, Ian W.; Hughes, David L.
 CS Department of Process Research, Merck & Co., Inc., Rahway, NJ, 07065, USA
 SO Journal of Organic Chemistry (2004), 69(22), 7761-7764
 CODEN: JOCEAH; ISSN: 0022-3263
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 141:424102
 GI



I



II



III

AB An efficient synthesis of o-nitrobenzylcarbonyl compds. by the Swern-type oxidation of readily accessible phenethanol analogs is reported. Reductive cyclization of o-nitrobenzylcarbonyl quinoline I [R = 4-(methylsulfonyl)piperazin-1-yl] using catalytic Raney nickel gives 1H-indol-2-yl-1H-quinoline II in 95% yield. Hydrolysis of II affords the KDR kinase inhibitor III in quant. yield. The analogous procedure was applied for the synthesis of indolyl quinolines II (R = H, MeCO₂). The examination of the reductive cyclization reaction and optimization of conditions is described.

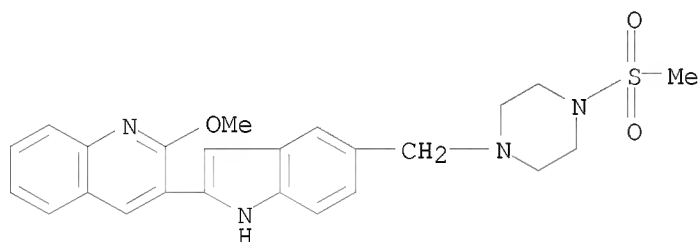
IT 796854-61-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of indolyl quinolines via catalytic reductive cyclization of nitrobenzylcarbonyl quinolines)

RN 796854-61-0 CAPLUS

CN Quinoline, 2-methoxy-3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



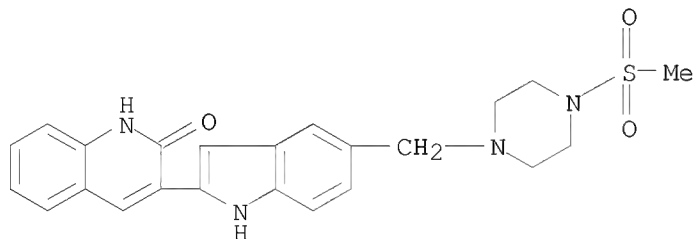
IT 415684-58-1P 796854-64-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of indolyl quinolines via catalytic reductive cyclization of nitrobenzylcarbonyl quinolines)

RN 415684-58-1 CAPLUS

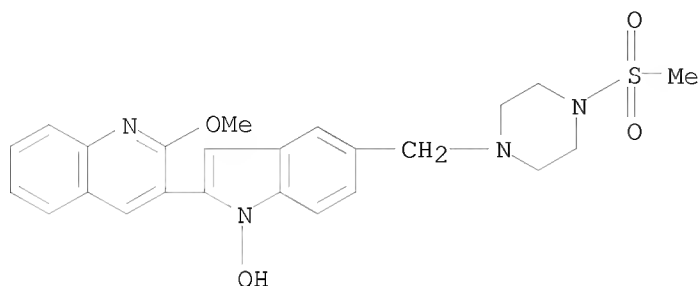
CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 796854-64-3 CAPLUS

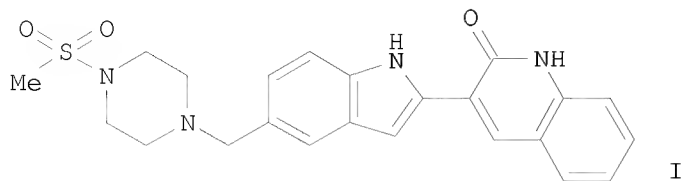
CN Quinoline, 3-[1-hydroxy-5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-2-methoxy- (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:855752 CAPLUS
DN 139:354459
TI Solid forms of 3-[5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one hydrochloride salt with tyrosine kinase activity
IN Karki, Shyam B.; Payack, Joseph; Treemaneeekarn, Varaporn; Wang, Yaling; Sato, Yuichi
PA Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2003088900 | A2 | 20031030 | WO 2003-US11022 | 20030411 |
| | WO 2003088900 | A3 | 20040521 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | CA 2480325 | A1 | 20031030 | CA 2003-2480325 | 20030411 |
| | AU 2003226051 | A1 | 20031103 | AU 2003-226051 | 20030411 |
| | JP 2005528400 | T | 20050922 | JP 2003-585653 | 20030411 |
| | US 20050113577 | A1 | 20050526 | US 2004-506710 | 20040907 |
| PRAI | US 2002-372782P | P | 20020416 | | |
| | WO 2003-US11022 | W | 20030411 | | |
| GI | | | | | |

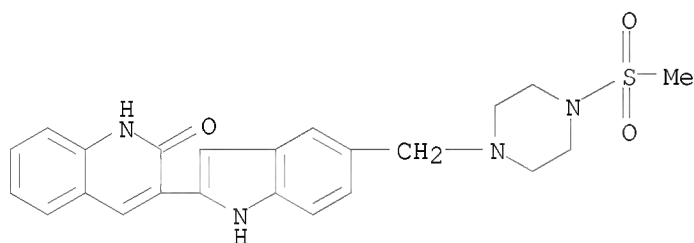


AB The present invention relates to solid forms of the I.HCl of which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals. I and its HCl salt were prepared and crystal forms were obtained and characterized.

IT 415684-58-1P
 RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (solid forms of 3-[5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one hydrochloride salt with tyrosine kinase activity)

RN 415684-58-1 CAPLUS

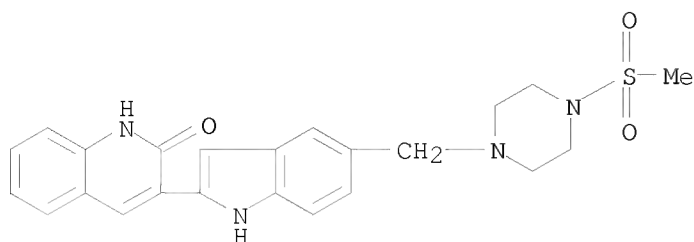
CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)



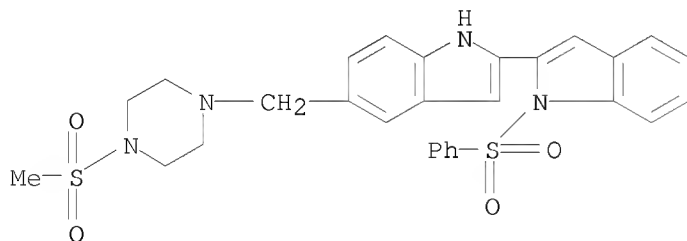
IT 335649-90-6P, 3-[5-(4-Methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (solid forms of 3-[5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one hydrochloride salt with tyrosine kinase activity)

RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



L6 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:685337 CAPLUS
 DN 139:338143
 TI Effective Strategy for the Preparation of Indolocarbazole Aglycons and Glycosides: Total Synthesis of Tjipanazoles B, D, E, and I
 AU Kuethe, Jeffrey T.; Wong, Audrey; Davies, Ian W.
 CS Department of Process Research, Merck Co., Inc., Rahway, NJ, 07065, USA
 SO Organic Letters (2003), 5(20), 3721-3723
 CODEN: ORLEF7; ISSN: 1523-7060
 PB American Chemical Society
 DT Journal
 LA English
 OS CASREACT 139:338143
 AB An effective strategy has been developed for the rapid and efficient preparation of ortho-nitrostyrenes, which can be converted to unsym. 2,2'-biindoles. A unique condensation of these 2,2'-biindoles with (dimethylamino)-acetaldehyde di-Et acetal affords the indolocarbazole ring system of the tjipanazole aglycon alkaloids in three synthetic steps and good to excellent overall yield. The first total synthesis of the tjipanazole glycoside alkaloids B and E is also discussed.
 IT 615552-46-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of unsym. 2,2'-biindoles from o-nitrostyrenes. which can be elaborated into indolocarbazole aglycons or indolopyrrolocarbazoles)
 RN 615552-46-0 CAPLUS
 CN 2,2'-Bi-1H-indole, 5'-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1-(phenylsulfonyl)- (CA INDEX NAME)

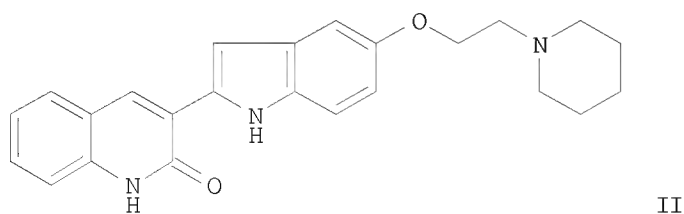
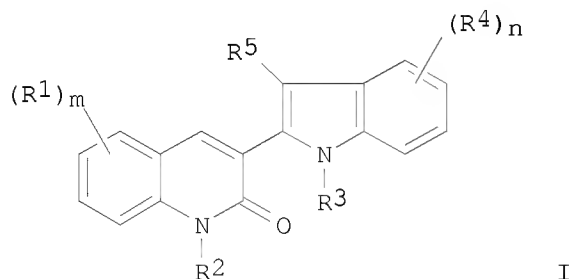


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

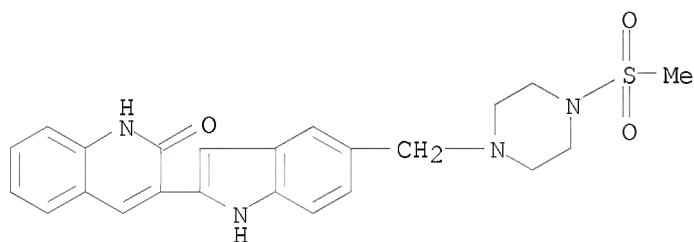
L6 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:202621 CAPLUS

DN 138:238027
 TI Preparation of 3-(2-indolyl)quinolin-2(1H)-ones as tyrosine kinase inhibitors
 IN Peckham, Jennifer P.; Hoffman, William F.; Arrington, Kenneth L.; Fraley, Mark E.; Hartman, George D.; Kim, Yuntae; Hanney, Barbara; Spencer, Keith L.
 PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 143 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

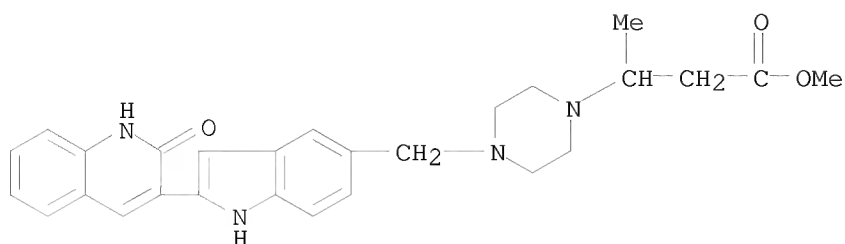
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2003020699 | A2 | 20030313 | WO 2002-US27114 | 20020826 |
| | WO 2003020699 | A3 | 20030522 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | AU 2002323406 | A1 | 20030318 | AU 2002-323406 | 20020826 |
| | US 20040235826 | A1 | 20041125 | US 2004-487589 | 20040224 |
| | US 7186723 | B2 | 20070306 | | |
| PRAI | US 2001-316123P | P | 20010830 | | |
| | WO 2002-US27114 | W | 20020826 | | |
| GI | | | | | |



- AB Title compds., including I (R groups undefined), were prepared and inhibitors, regulators, and/or modulators of tyrosine kinase signal transduction. For example, 1-(tert-butoxycarbonyl)-5-[(tert-butyldimethylsilyl)oxy]-1H-indol-2-ylboronic acid was coupled with 2-chloro-3-iodoquinoline (preparation of starting materials given) in the presence of Pd(PPh₃)₄ and K₃PO₄ in dioxane to give the protected 3-(2-indolyl)quinoline derivative. Deprotection using triethylamine trihydrofluoride afforded the alc. Reaction with 1-(2-chloroethyl)piperidine•HCl and Cs₂CO₃ in DMF followed by reflux at 110° in AcOH and H₂O for 12 h provided II. Compds. of the invention inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC₅₀ values between 0.01 μM - 5.0 μM. Thus, I and compns. containing I are useful for the treatment of tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals (no data).
- IT 335649-90-6P, 3-[5-[(4-Methanesulfonylpiperazin-1-yl)methyl]-1H-indol-2-yl]-1H-quinolin-2-one
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of (indolyl)quinolinones for treatment of cancer, atherosclerosis, inflammatory diseases, and other tyrosine kinase-dependent conditions)
- RN 335649-90-6 CAPLUS
- CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



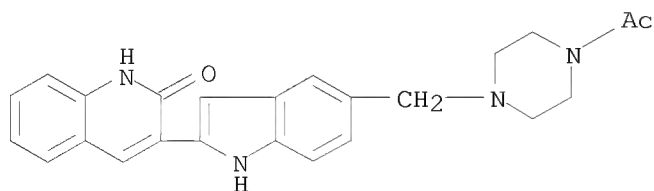
- IT 501334-37-8, 3-[4-[[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-5-yl]methyl]piperazin-1-yl]butyric acid methyl ester
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of (indolyl)quinolinones for treatment of cancer, atherosclerosis, inflammatory diseases, and other tyrosine kinase-dependent conditions)
- RN 501334-37-8 CAPLUS
- CN 1-Piperazinepropanoic acid, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]-β-methyl-, methyl ester (CA INDEX NAME)



IT 335649-92-8P, 3-[5-[(4-Acetylpiperazin-1-yl)methyl]-1H-indol-2-yl]-1H-quinolin-2-one 335649-94-0P, 3-[5-(Piperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one 335649-95-1P, 3-[5-[[4-(2-Hydroxyethanoyl)piperazin-1-yl]methyl]-1H-indol-2-yl]-1H-quinolin-2-one 335650-03-8P, 4-(2-Carboxyl-1-methylethyl)-1-[[2-(2-oxo-1,2-dihydroquinolin-3-yl)-1H-indol-5-yl]methyl]piperazine trifluoroacetate (1:1) 501334-36-7P 501334-49-2P, 3-[5-[[[(3S)-3-Methylpiperazin-1-yl)methyl]-1H-indol-2-yl]quinolin-2(1H)-one 501334-50-5P, 3-[5-[[[(3R)-3-Methylpiperazin-1-yl)methyl]-1H-indol-2-yl]quinolin-2(1H)-one 501334-51-6P, 3-[5-[[[(3S)-3-Methyl-4-(methylsulfonyl)piperazin-1-yl]methyl]-1H-indol-2-yl]quinolin-2(1H)-one 501334-52-7P, 3-[5-[[[(3R)-3-Methyl-4-(methylsulfonyl)piperazin-1-yl]methyl]-1H-indol-2-yl]quinolin-2(1H)-one 501334-54-9P, 3-[5-[[4-(1,1-Dioxotetrahydrothien-3-yl)piperazin-1-yl]methyl]-1H-indol-2-yl]quinolin-2(1H)-one 501334-56-1P, 2-[4-[[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-5-yl]methyl]piperazin-1-yl]acetamide 501334-65-2P, 4-[[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-5-yl]methyl]piperazine-1-carboxamide 501334-72-1P, 1-[[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-5-yl]methyl]piperazine-2-carboxamide 501334-73-2P, 4-[[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-5-yl]methyl]piperazine-2-carboxamide 501334-74-3P, 3-[5-[[3-Oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl]methyl]-1H-indol-2-yl]quinolin-2(1H)-one 501334-93-6P, 3-[6-[[4-(Methylsulfonyl)piperazin-1-yl]methyl]-1H-indol-2-yl]quinolin-2(1H)-one
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (tyrosine kinase inhibitor; preparation of (indolyl)quinolinones for treatment of cancer, atherosclerosis, inflammatory diseases, and other tyrosine kinase-dependent conditions)

RN 335649-92-8 CAPLUS

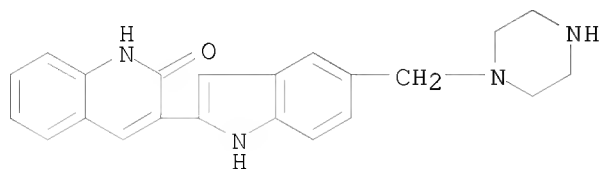
CN 2(1H)-Quinolinone, 3-[5-[(4-acetyl-1-piperazinyl)methyl]-1H-indol-2-yl]-
 (CA INDEX NAME)



RN 335649-94-0 CAPLUS

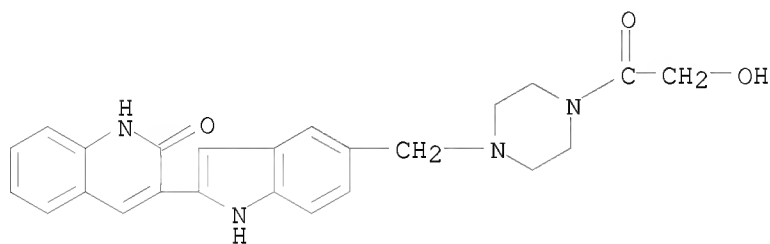
10/557537-Part I

CN 2(1H)-Quinolinone, 3-[5-(1-piperazinylmethyl)-1H-indol-2-yl]- (CA INDEX NAME)



RN 335649-95-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(2-hydroxyacetyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



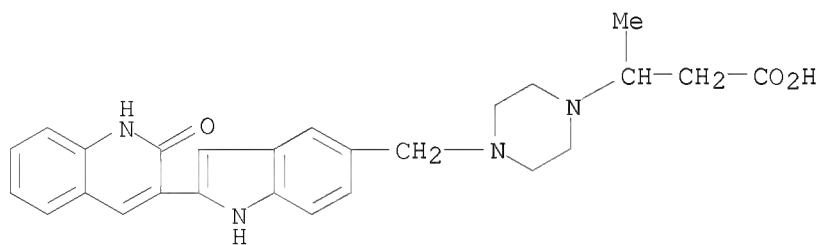
RN 335650-03-8 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]-β-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 335650-02-7

CMF C26 H28 N4 O3

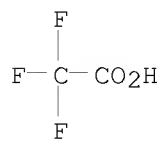


CM 2

CRN 76-05-1

CMF C2 H F3 O2

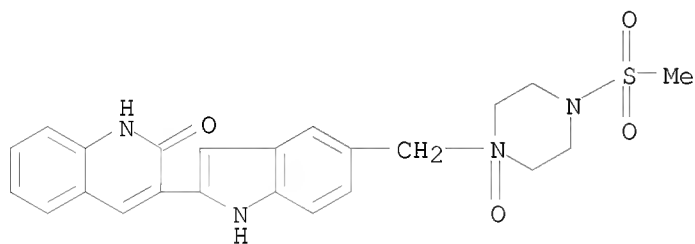
10/557537-Part I



RN 501334-36-7 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-oxido-1-piperazinyl]methyl]-1H-indol-2-yl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

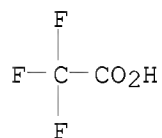
CM 1

CRN 335649-91-7
CMF C23 H24 N4 O4 S



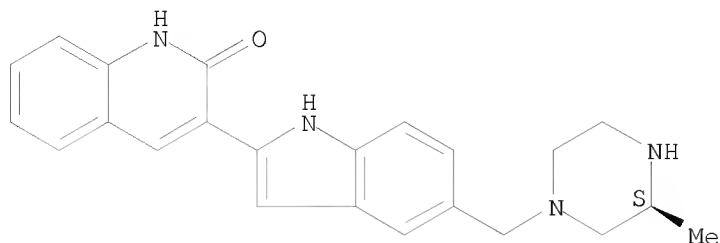
CM 2

CRN 76-05-1
CMF C2 H F3 O2



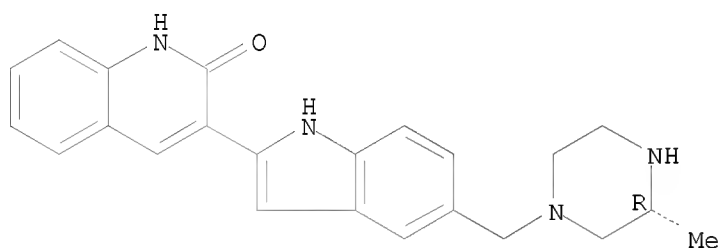
RN 501334-49-2 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-[[[(3S)-3-methyl-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

Absolute stereochemistry.



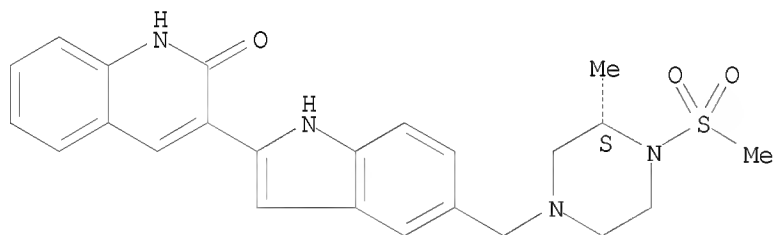
RN 501334-50-5 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[(3R)-3-methyl-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

Absolute stereochemistry.



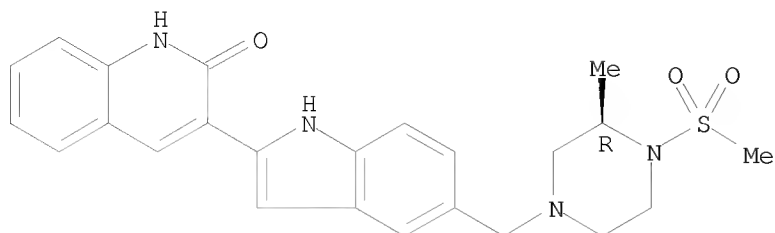
RN 501334-51-6 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[(3S)-3-methyl-4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

Absolute stereochemistry.



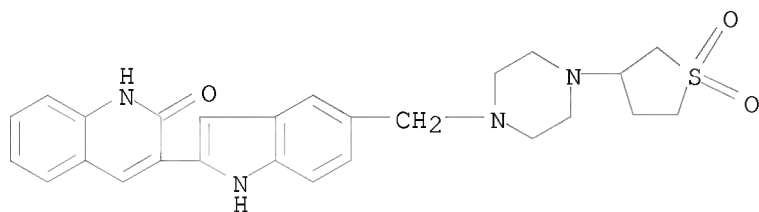
RN 501334-52-7 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[(3R)-3-methyl-4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)

Absolute stereochemistry.



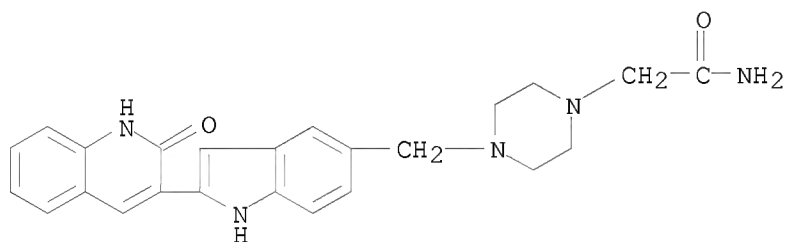
RN 501334-54-9 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(tetrahydro-1,1-dioxido-3-thienyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



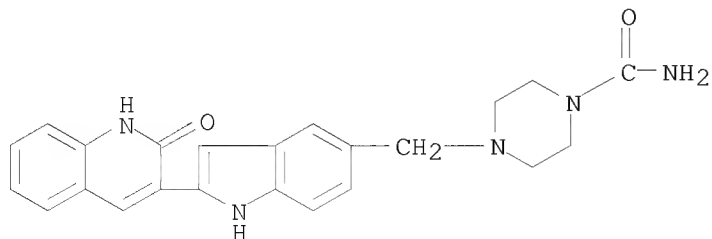
RN 501334-56-1 CAPLUS

CN 1-Piperazineacetamide, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]- (CA INDEX NAME)



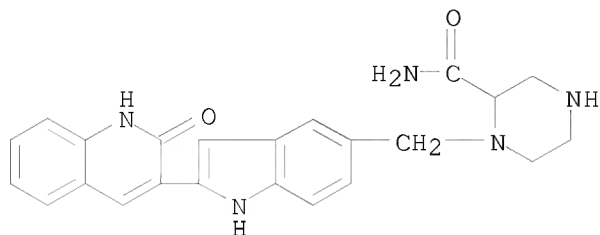
RN 501334-65-2 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]- (CA INDEX NAME)



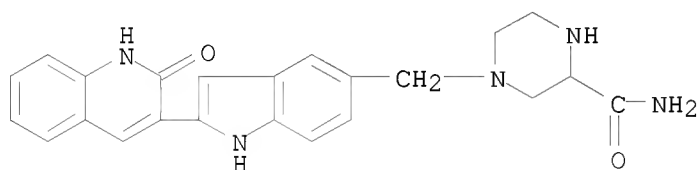
RN 501334-72-1 CAPLUS

CN 2-Piperazinecarboxamide, 1-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]- (CA INDEX NAME)



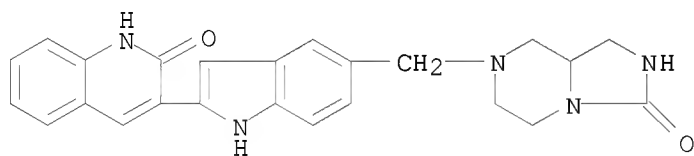
RN 501334-73-2 CAPLUS

CN 2-Piperazinecarboxamide, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]- (CA INDEX NAME)



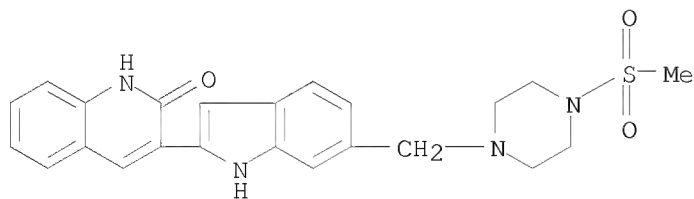
RN 501334-74-3 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[(hexahydro-3-oxoimidazo[1,5-a]pyrazin-7(1H)-yl)methyl]-1H-indol-2-yl]- (CA INDEX NAME)



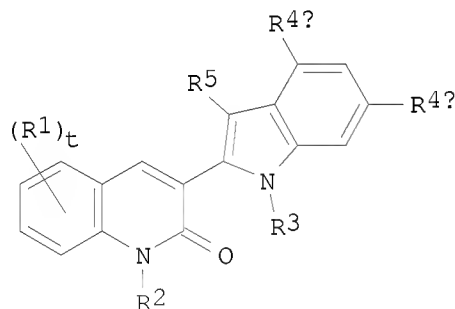
RN 501334-93-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[6-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



L6 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:202476 CAPLUS
 DN 138:238026
 TI Preparation of indolinylnquinolinones as tyrosine kinase inhibitors with
 therapeutic uses
 IN Kim, Yuntae; Hanney, Barbara; Spencer, Keith L.; Hartman, George D.;
 Arrington, Kenneth L.
 PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 90 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2003020276 | A1 | 20030313 | WO 2002-US27161 | 20020826 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2002326760 | A1 | 20030318 | AU 2002-326760 | 20020826 |
| | US 20040192725 | A1 | 20040930 | US 2004-487588 | 20040224 |
| | US 6927293 | B2 | 20050809 | | |
| PRAI | US 2001-315897P | P | 20010830 | | |
| | WO 2002-US27161 | W | 20020826 | | |
| OS | MARPAT 138:238026 | | | | |
| GI | | | | | |



I

AB The present invention relates to indolinylnquinolinones (shown as I; variables defined below; e.g. 3-[6-[(4-methylpiperazin-1-yl)carbonyl]-1H-indol-2-yl]quinolin-2(1H)-one) which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals. For I: a = 0 or 1; b = 0 or 1; n = 0,

1, or 2; t = 1 or 2; R1 and R5 = H, (C:O)aObC1-C10 alkyl, (C:O)aObaryl, (C:O)aObC2-C10 alkenyl, (C:O)aObC2-C10 alkynyl, CO2H, halo, OH, ObC1-C6 perfluoroalkyl, (C:O)aNR7R8, CN, (C:O)aObC3-C8 cycloalkyl, and (C:O)aObheterocyclyl. R2 and R3 = H, (C:O)OaC1-C6 alkyl, (C:O)Oaaryl, C1-C6 alkyl, SO2Ra, and aryl; R4a or R4b = H and the other = (C:O)aObC1-C10 alkyl, (C:O)aObaryl, (C:O)aObC2-C10 alkenyl, (C:O)aObC2-C10 alkynyl, CO2H, halo, OH, ObC1-C6 perfluoroalkyl, (C:O)aNR7R8, CN, (C:O)aObC3-C8 cycloalkyl, and (C:O)aObheterocyclyl. R7 and R8 = H, (C:O)ObC1-C10 alkyl, (C:O)ObC3-C8 cycloalkyl, (C:O)Obaryl, (C:O)Obheterocyclyl, C1-C10 alkyl, aryl, C2-C10 alkenyl, C2-C10 alkynyl, heterocyclyl, C3-C8 cycloalkyl, SO2Ra, (C:O)N(Rb)2, or R7 and R8 can be taken together with the N to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the N, one or two addnl. heteroatoms = N, O and S;

Ra

= (C1-C6)alkyl, (C3-C6)cycloalkyl, aryl, or heterocyclyl; and Rb is H, (C1-C6)alkyl, aryl, heterocyclyl, (C3-C6)cycloalkyl, (C:O)OC1-C6 alkyl, (C:O)C1-C6 alkyl or S(O)2Ra. Compds. I inhibit VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values = 0.01-5.0 μ M. Although the methods of preparation are not claimed, 3 example preps. are included.

IT

501334-93-6P, 3-[6-[[4-(Methylsulfonyl)piperazin-1-yl]methyl]-1H-indol-2-yl]quinolin-2(1H)-one 501364-54-1P, 3-[3-Fluoro-5-(4-methanesulfonylpiperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one 501364-55-2P, 4-[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-6-ylmethyl]piperazine-1-carboxylic acid methylamide 501364-56-3P, 3-[4-[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-6-ylmethyl]piperazin-1-yl]butyric acid 501364-57-4P, 3-[4-(4-Methanesulfonylpiperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one 501364-58-5P, 3-[4-[2-(2-Oxo-1,2-dihydroquinolin-3-yl)-1H-indol-4-ylmethyl]piperazin-1-yl]butyric acid 501364-59-6P, 3-[3-Fluoro-6-(4-methanesulfonylpiperazin-1-ylmethyl)-1H-indol-2-yl]-1H-quinolin-2-one 501364-60-9P, 4-[[3-Fluoro-2-(2-oxo-1,2-dihydroquinolin-3-yl)-1H-indol-6-yl]methyl]piperazine-1-carboxylic acid methylamide 501364-61-0P, 3-[4-[3-Fluoro-2-(2-oxo-1,2-dihydroquinolin-3-yl)-1H-indol-6-ylmethyl]piperazin-1-yl]butyric acid 501364-62-1P, 3-[3-Fluoro-4-[(4-methanesulfonylpiperazin-1-yl)methyl]-1H-indol-2-yl]-1H-quinolin-2-one 501364-63-2P, 3-[4-[[3-Fluoro-2-(2-oxo-1,2-dihydroquinolin-3-yl)-1H-indol-4-yl]methyl]piperazin-1-yl]butyric acid
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

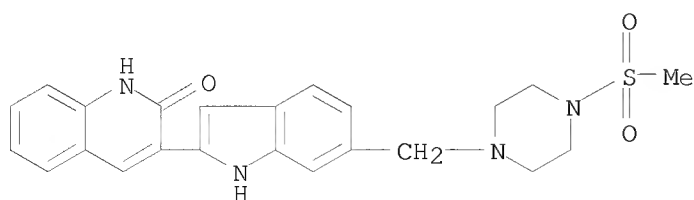
(drug candidate; preparation of indolinylquinolinones as tyrosine kinase inhibitors with therapeutic uses)

RN

501334-93-6 CAPLUS

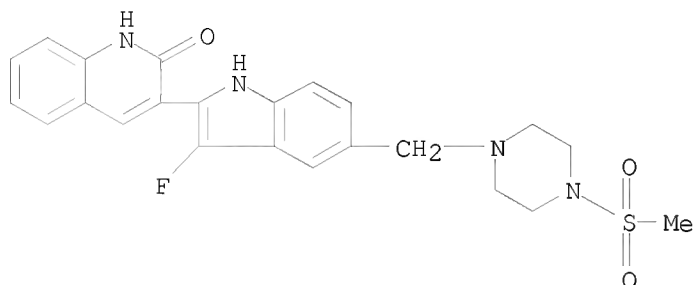
CN

2(1H)-Quinolinone, 3-[6-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



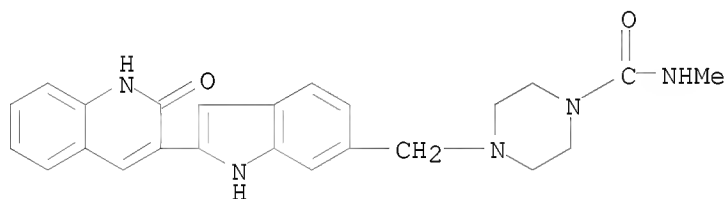
RN 501364-54-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[3-fluoro-5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



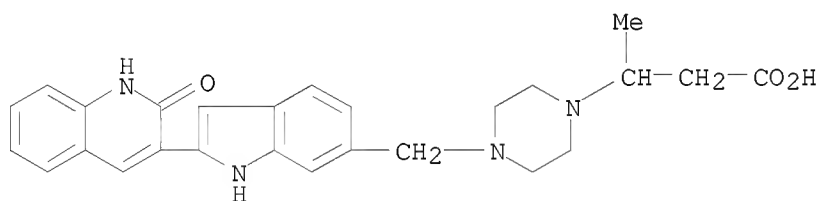
RN 501364-55-2 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-6-yl]methyl]-N-methyl- (CA INDEX NAME)



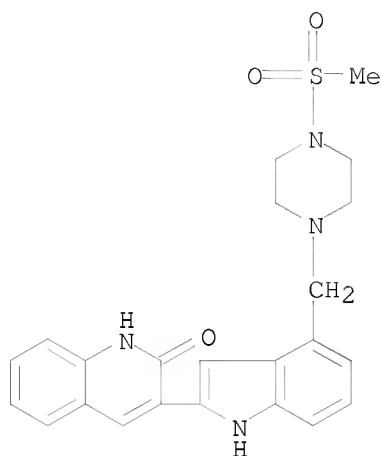
RN 501364-56-3 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-6-yl]methyl]-β-methyl- (CA INDEX NAME)



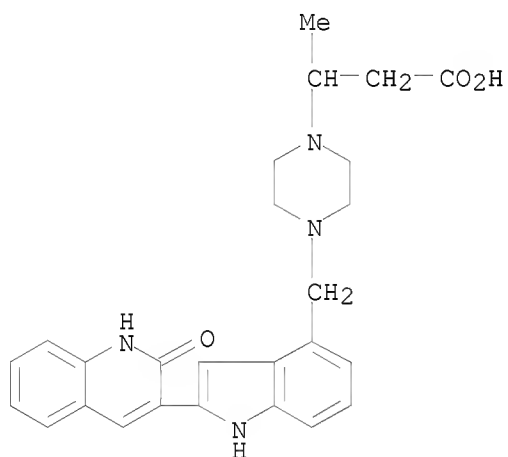
RN 501364-57-4 CAPLUS

CN 2(1H)-Quinolinone, 3-[4-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



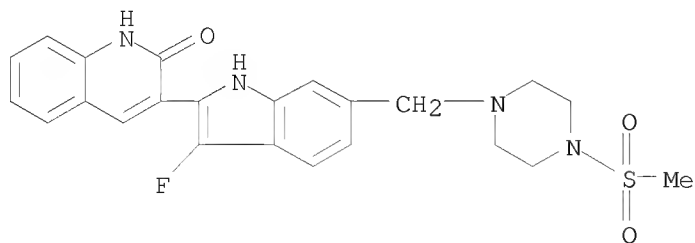
RN 501364-58-5 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-4-yl]methyl]-β-methyl- (CA INDEX NAME)



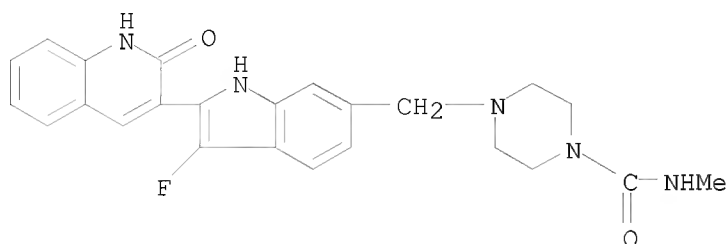
RN 501364-59-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[3-fluoro-6-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



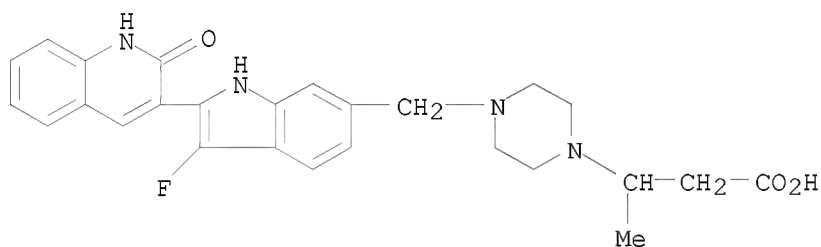
RN 501364-60-9 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-3-fluoro-1H-indol-6-yl]methyl]-N-methyl- (CA INDEX NAME)



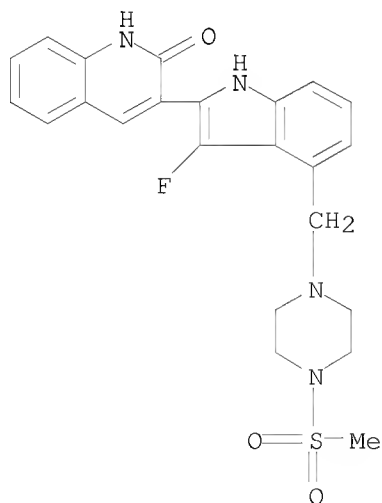
RN 501364-61-0 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-3-fluoro-1H-indol-6-yl]methyl]-β-methyl- (CA INDEX NAME)



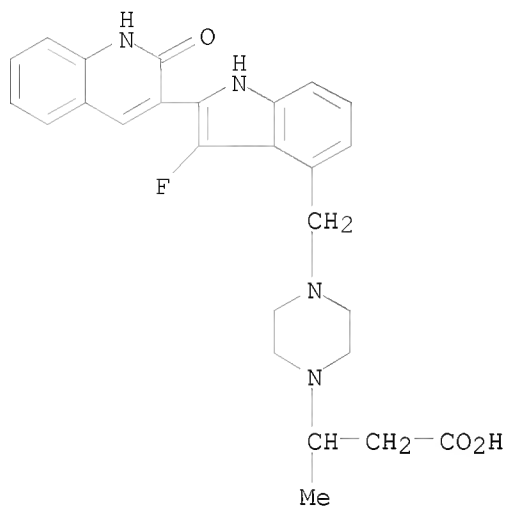
RN 501364-62-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[3-fluoro-4-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 501364-63-2 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-3-fluoro-1H-indol-4-yl]methyl]- β -methyl- (CA INDEX NAME)



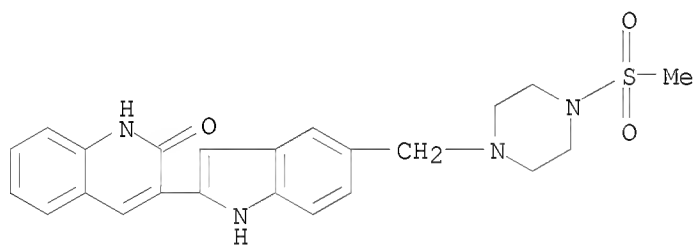
IT 335649-90-6, 3-[5-[[4-(Methylsulfonyl)piperazin-1-yl]methyl]-1H-indol-2-yl]quinolin-2(1H)-one

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of indolinylquinolinones as tyrosine kinase inhibitors with therapeutic uses)

RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:314903 CAPLUS

DN 136:325437

TI Preparation of oxoquinolinylindole-5-methanamine salts as tyrosine kinase signal transduction modulators

IN Fraley, Mark E.; Karki, Shyam B.; Kim, Yuntae

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 73 pp.

CODEN: PIXXD2

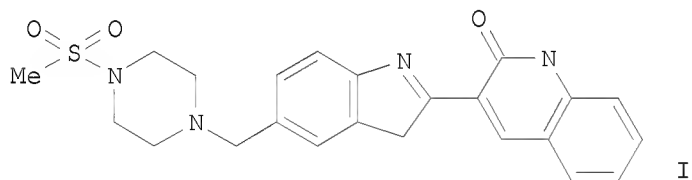
DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2002032861 | A2 | 20020425 | WO 2001-US32508 | 20011017 |
| | WO 2002032861 | A3 | 20020815 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | CA 2424689 | A1 | 20020425 | CA 2001-2424689 | 20011017 |
| | AU 2002026877 | A | 20020429 | AU 2002-26877 | 20011017 |
| | US 20020072526 | A1 | 20020613 | US 2001-981979 | 20011017 |
| | US 6656942 | B2 | 20031202 | | |
| | EP 1328519 | A2 | 20030723 | EP 2001-987742 | 20011017 |
| | EP 1328519 | B1 | 20050907 | | |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| | JP 2004511541 | T | 20040415 | JP 2002-536045 | 20011017 |
| | AT 303998 | T | 20050915 | AT 2001-987742 | 20011017 |
| | AU 2002226877 | B2 | 20060112 | AU 2002-226877 | 20011017 |
| | ES 2247187 | T3 | 20060301 | ES 2001-987742 | 20011017 |
| | US 20040002501 | A1 | 20040101 | US 2003-398851 | 20030410 |
| | US 6960590 | B2 | 20051101 | | |
| PRAI | US 2000-241043P | P | 20001017 | | |
| | WO 2001-US32508 | W | 20011017 | | |

GI



AB Title compds. were prepared as tyrosine kinase signal transduction modulators (no data). Thus, di-protected 5-hydroxymethylindole-2-boronic acid was condensed with 3-iodo-2-quinolinone (preparation each given) and the O-deprotected product oxidized to the aldehyde which was reductively aminated by 1-methanesulfonylpiperazine to give, after deprotection and salt formation, title compound I.MeSO₃H.

IT 335649-90-6P 335649-95-1P 415684-56-9P
 415684-57-0P 415684-58-1P 415684-59-2P
 415684-60-5P 415684-61-6P 415684-62-7P

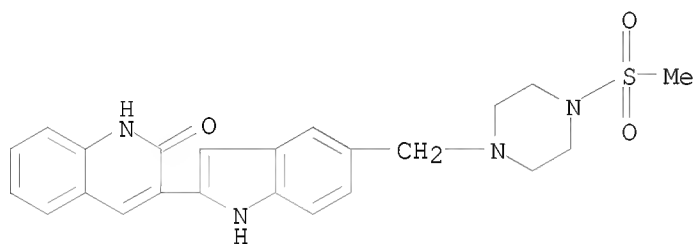
415684-63-8P 415684-64-9P 415684-68-3P
415684-69-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of oxoquinolinylindole-5-methanamine salts as tyrosine kinase
signal transduction modulators)

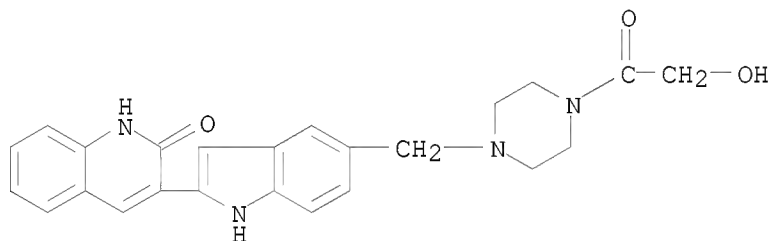
RN 335649-90-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-
indol-2-yl]- (CA INDEX NAME)



RN 335649-95-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(2-hydroxyacetyl)-1-piperazinyl]methyl]-1H-
indol-2-yl]- (CA INDEX NAME)



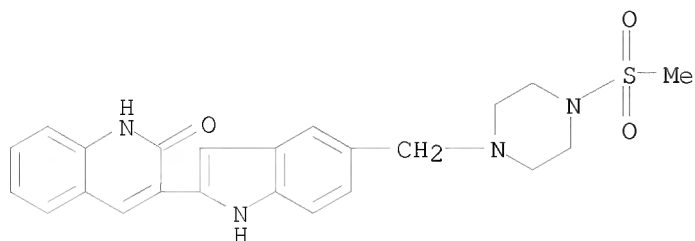
RN 415684-56-9 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-
indol-2-yl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 335649-90-6

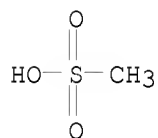
CMF C23 H24 N4 O3 S



CM 2

CRN 75-75-2

CMF C H4 O3 S



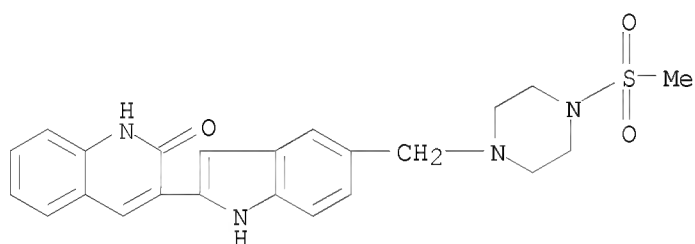
RN 415684-57-0 CAPLUS

CN Piperazine, 1-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]-4-(methylsulfonyl)-, (2R,3R)-2,3-dihydroxybutanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 335649-90-6

CMF C23 H24 N4 O3 S

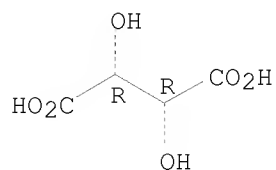


CM 2

CRN 87-69-4

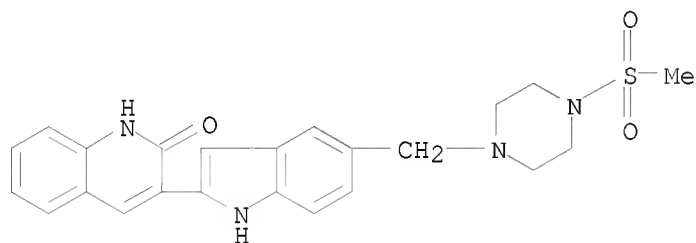
CMF C4 H6 O6

Absolute stereochemistry.



RN 415684-58-1 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

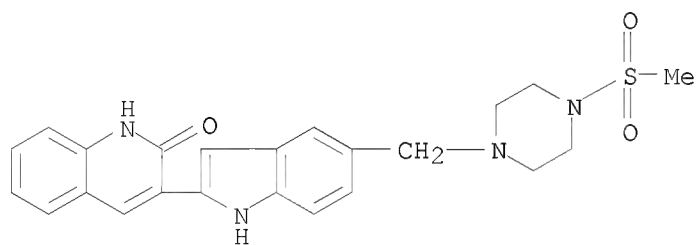
RN 415684-59-2 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, 2-hydroxy-1,2,3-propanetricarboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 335649-90-6

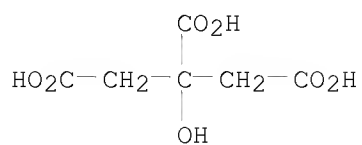
CMF C23 H24 N4 O3 S



CM 2

CRN 77-92-9

CMF C6 H8 O7



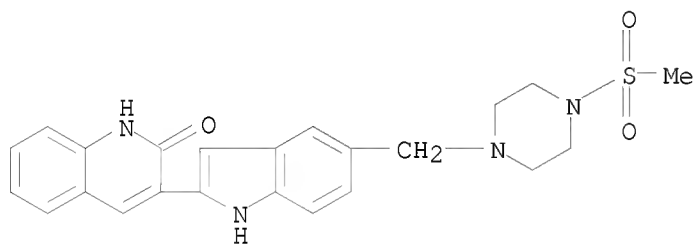
RN 415684-60-5 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, acetate (1:1) (CA INDEX NAME)

CM 1

CRN 335649-90-6

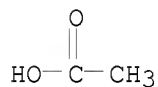
CMF C23 H24 N4 O3 S



CM 2

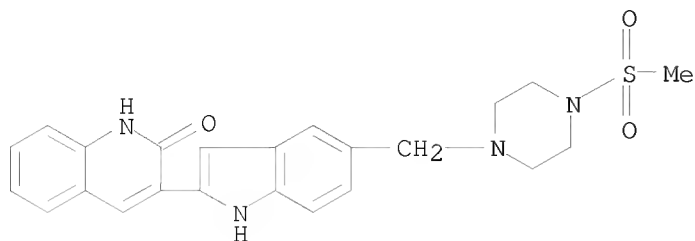
CRN 64-19-7

CMF C2 H4 O2



RN 415684-61-6 CAPLUS

CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, hydrobromide (1:1) (CA INDEX NAME)

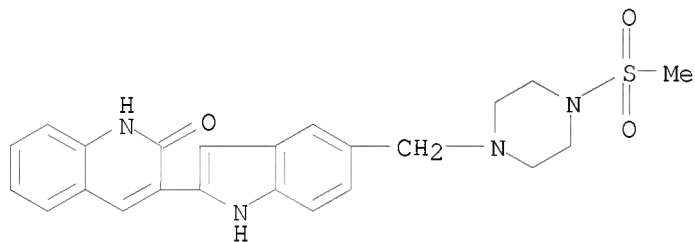


● HBr

RN 415684-62-7 CAPLUS
 CN Piperazine, 1-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]-4-(methylsulfonyl)-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

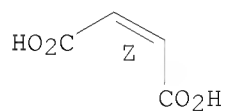
CRN 335649-90-6
 CMF C23 H24 N4 O3 S



CM 2

CRN 110-16-7
 CMF C4 H4 O4

Double bond geometry as shown.

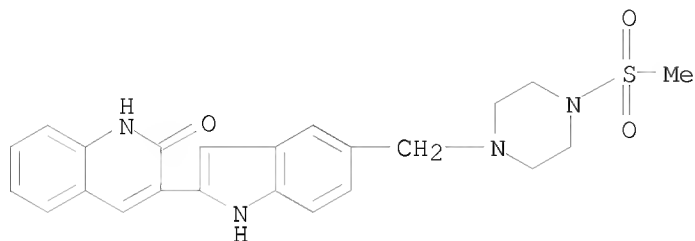


RN 415684-63-8 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, sulfate (1:?) (CA INDEX NAME)

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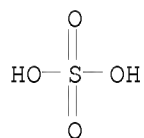
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CRN 335649-90-6
CMF C23 H24 N4 O3 S



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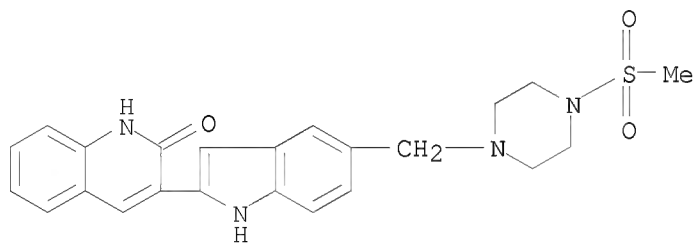
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CMF H2 O4 S



RN 415684-64-9 CAPLUS
CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]-, benzenesulfonate (1:1) (CA INDEX NAME)

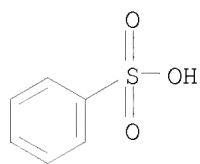
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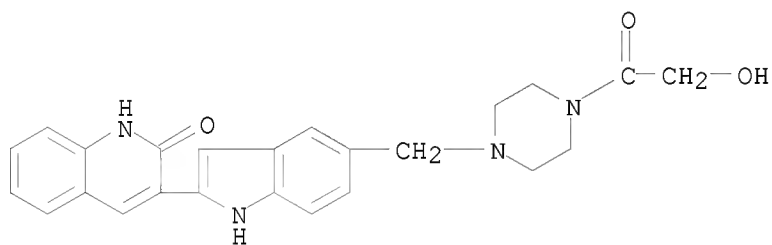
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RN 415684-68-3 CAPLUS
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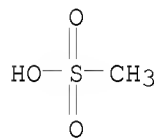
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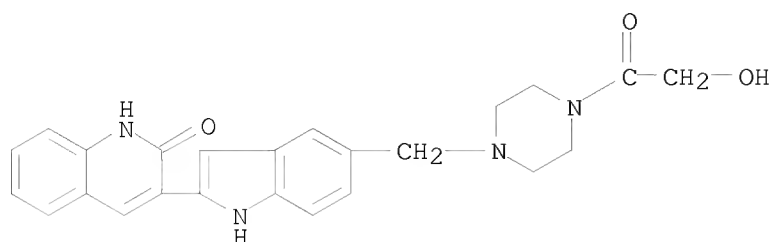


CM 2

CRN 75-75-2
 CMF C H4 O3 S



RN 415684-69-4 CAPLUS
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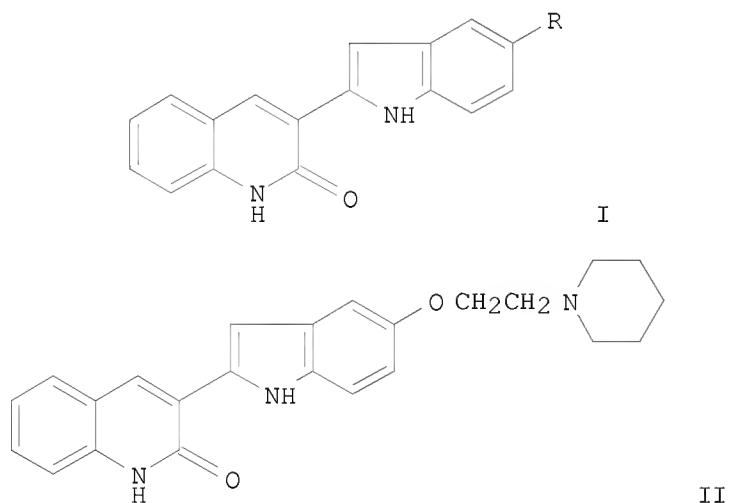


● HCl

L6 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2001:300706 CAPLUS
 DN 134:326411
 TI Preparation of 3-(2-indolyl)quinoline-2-one derivatives as tyrosine kinase inhibitors
 IN Arrington, Kenneth L.; Bilodeau, Mark T.; Fraley, Mark E.; Hartman, George D.; Hoffman, William F.; Hungate, Randall W.; Kim, Yuntae
 PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 130 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2001029025 | A2 | 20010426 | WO 2000-US28625 | 20001016 |
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| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| | CA 2387351 | A1 | 20010426 | CA 2000-2387351 | 20001016 |
| | BR 2000014843 | A | 20020611 | BR 2000-14843 | 20001016 |
| | EP 1226136 | A2 | 20020731 | EP 2000-978230 | 20001016 |
| | EP 1226136 | B1 | 20041229 | | |
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| | TR 200201051 | T2 | 20020923 | TR 2002-1051 | 20001016 |
| | HU 2002003323 | A2 | 20030228 | HU 2002-3323 | 20001016 |
| | HU 2002003323 | A3 | 20040128 | | |
| | JP 2003512369 | T | 20030402 | JP 2001-531825 | 20001016 |
| | JP 3822494 | B2 | 20060920 | | |
| | EE 200200201 | A | 20030616 | EE 2002-201 | 20001016 |
| | NZ 518001 | A | 20040528 | NZ 2000-518001 | 20001016 |
| | AU 778588 | B2 | 20041209 | AU 2001-15710 | 20001016 |

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| AT 286045 | T | 20050115 | AT 2000-978230 | 20001016 |
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| ES 2234698 | T3 | 20050701 | ES 2000-978230 | 20001016 |
| US 6306874 | B1 | 20011023 | US 2000-690598 | 20001017 |
| TW 239957 | B | 20050921 | TW 2000-89121943 | 20001019 |
| ZA 2002002985 | A | 20030416 | ZA 2002-2985 | 20020416 |
| NO 2002001820 | A | 20020523 | NO 2002-1820 | 20020418 |
| MX 2002PA03887 | A | 20020930 | MX 2002-PA3887 | 20020418 |
| US 6794393 | B1 | 20040921 | US 2002-110872 | 20020418 |
| BG 106710 | A | 20030331 | BG 2002-106710 | 20020516 |
| HK 1054931 | A1 | 20060317 | HK 2003-107148 | 20031003 |
| US 20050096344 | A1 | 20050505 | US 2004-900662 | 20040728 |
| JP 2006206609 | A | 20060810 | JP 2006-127244 | 20060501 |
| PRAI US 1999-160356P | P | 19991019 | | |
| JP 2001-531825 | A3 | 20001016 | | |
| WO 2000-US28625 | W | 20001016 | | |
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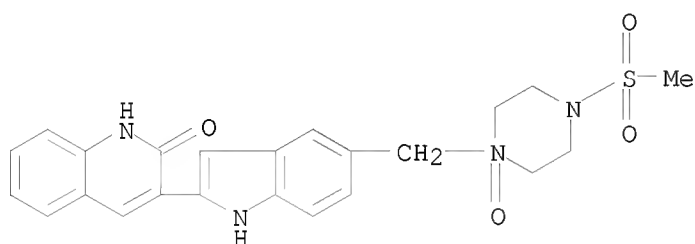
AB Title compds. [I; R = (CH₃)₂NCH₂CH(CH₃)CH₂O, (CH₃OCH₂CH₂)(C₆H₅CH₂)NCH₂CH₂O, (CH₃CH₂)₂NCH₂CH₂O, (CH₃)(C₆H₅CH₂)NCH₂CH₂CH₂O, (CH₃OCH₂CH₂)(HOOCCH₂CH₂)NCH₂CH₂O, (CH₃OCH₂CH₂)(CH₃SO₂)NCH₂, cycloalkylaminoalkyl, heterocyclylalkyl, etc.], stereoisomer, and pharmaceutically acceptable salts are prepared and inhibit, regulate and/or modulate tyrosine kinase signal transduction. Title compds. are tested on VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC₅₀ values between 0.001-5.0 μ M. Pharmaceutical compns. and methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, etc. are discussed. Thus, the title compound II was prepared

IT 335649-91-7P 335649-92-8P 335649-94-0P
335649-95-1P 335650-03-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-(2-indolyl)quinoline-2-one derivs. as tyrosine kinase inhibitors)

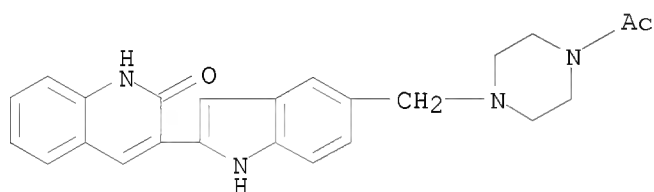
RN 335649-91-7 CAPLUS

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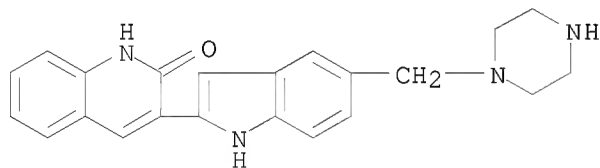
RN 335649-92-8 CAPLUS

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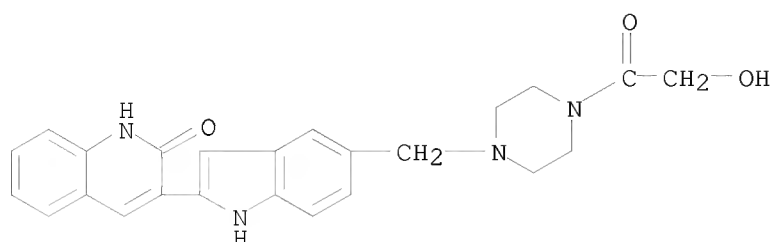
RN 335649-94-0 CAPLUS

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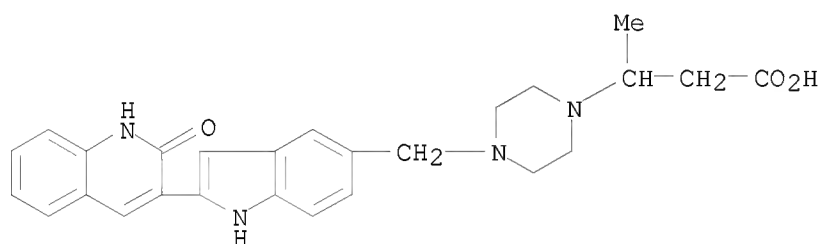
CN 2(1H)-Quinolinone, 3-[5-[[4-(2-hydroxyacetyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



RN 335650-03-8 CAPLUS
 CN 1-Piperazinepropanoic acid, 4-[[2-(1,2-dihydro-2-oxo-3-quinolinyl)-1H-indol-5-yl]methyl]-β-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

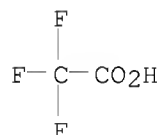
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 CMF C26 H28 N4 O3

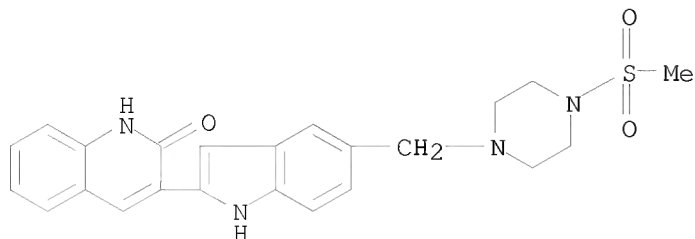


CM 2

CRN 76-05-1
 CMF C2 H F3 O2



IT 335649-90-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of 3-(2-indolyl)quinoline-2-one derivs. as tyrosine kinase inhibitors)
 RN 335649-90-6 CAPLUS
 CN 2(1H)-Quinolinone, 3-[5-[[4-(methylsulfonyl)-1-piperazinyl]methyl]-1H-indol-2-yl]- (CA INDEX NAME)



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COST IN U.S. DOLLARS

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SESSION

FULL ESTIMATED COST

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10/557537-Part I

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